Proposed Re-evaluation Decision PRVD2010-01

Tefluthrin

(publié aussi en français)

24 February 2010

This document is published by the Health Canada Pest Management Regulatory Agency. For further information, please contact:

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Canada

HC Pub: 100007

ISBN: 978-1-100-14618-8 (978-1-100-14619-5)
Catalogue number: H113-27/2010-1E (H113-27/2010-1E-PDF)

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Overview

Proposed Re-evaluation Decision for Tefluthrin

After a re-evaluation of the insecticide tefluthrin, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act*, is proposing continued registration of products containing tefluthrin for sale and use in Canada.

An evaluation of available scientific information found that products containing tefluthrin have value in the food and crop industry and do not present unacceptable risks to human health or the environment. As a condition of the continued registration of tefluthrin for use on field corn, sweet corn and seed corn, new risk reduction measures are proposed. Additional data are being requested.

The PMRA's pesticide re-evaluation program considers potential risks as well as the value of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure. Re-evaluation draws on data from registrants, published scientific reports, information from other regulatory agencies and any other relevant information available.

This proposal affects all end-use products containing tefluthrin registered in Canada. Once the final re-evaluation decision is made, registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for tefluthrin and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of tefluthrin.

The PMRA will accept written comments on this proposal up to 60 days from the date of publication of this document. Please forward all comments to Publications.

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

What Does Health Canada Consider When Making a Re-evaluation Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its conditions or proposed conditions of registration.[2] The Act also requires that products have value[3] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies hazard and risk assessment methods as well as policies that are rigorous and modern. These methods consider the unique characteristics of sensitive subpopulations in both humans (for example, children) and organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a re-evaluation decision on tefluthrin, the PMRA will consider all comments received from the public in response to this consultation document.[4] The PMRA will then publish a Re-evaluation Decision[5] on tefluthrin, which will include the decision, the reasons for it, a summary of comments received on the proposed registration decision and the PMRA's response to these comments.

For more details on the information presented in this overview, please refer to the Science Evaluation in this consultation document.

What Is Tefluthrin?

Tefluthrin is a synthetic pyrethroid insecticide (Resistance Management Mode of Action (MoA) Group 3), registered to control northern corn rootworm, western corn rootworm, black cutworm, wireworm and seedcorn maggot in field corn, sweet corn and seed corn. It is applied to the soil at planting using conventional ground equipment by farmers, farm workers and professional applicators.

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2 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

3 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's *(a)* efficacy; *(b)* effect on host organisms in connection with which it is intended to be used; and *(c)* health, safety and environmental benefits and social and economic impact."

4 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

5 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Health Considerations

Can Approved Uses of Tefluthrin Affect Human Health?

Additional risk-reduction measures are required on tefluthrin labels. Tefluthrin is unlikely to affect your health when used according to the revised label directions.

Potential exposure to tefluthrin may occur through the diet (food and water), applying the product or, to a lesser extent, by entering treated sites. When assessing health risks, two key factors are considered: the dose levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only those uses where exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when tefluthrin products are used according to label directions.

Tefluthrin showed high acute toxicity to mice by the oral route of exposure and to rats by the oral, inhalation and dermal routes of exposure. In rabbits, tefluthrin was slightly to minimally irritating to the skin and was severely irritating to the eye. Tefluthrin was not a potential skin sensitizer in guinea pigs.

There was no evidence that tefluthrin was genotoxic or teratogenic. In female rats, there was evidence of carcinogenicity in the form of uterine adenocarcinomas. Benign liver tumours were observed in female mice. Tefluthrin did not cause cancer in male mice or rats. The major target organ for tefluthrin in repeat-dose toxicological testing was the nervous system with signs typical of pyrethroid toxicity reported in all species examined by the oral route and in rats examined by the dermal route. Tefluthrin's effect on organ weights and histopathology suggest that the liver is also a target organ in all examined species.

When tefluthrin was given to pregnant animals, an enhancement of clinical signs of neurotoxicity was noted with multigenerational exposure. Based on evidence of neurotoxicity in the offspring in the absence of parental toxicity, there is a sensitivity of the young animal to tefluthrin. Additional studies are required.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Occupational Risks from Handling Tefluthrin

Occupational risks are not of concern.

Occupational risks (mixing, loading and applying product) are not of concern for agricultural scenarios, provided additional protective measures are followed. Based on the precautions and directions for use on the registered product labels, non-cancer risk estimates associated with certain mixing, loading and applying activities did not meet current standards and are of concern. However, the uses for agricultural scenarios will meet the targets when engineering controls and personal protective equipment are used. These measures are needed to minimize potential exposure and protect worker's health.

Cancer risks are not of concern.

Postapplication risks are not of concern.

Postapplication occupational risk assessments consider exposures to workers entering treated sites in agriculture. No data exists to adequately assess postapplication exposure to tefluthrin from areas treated with a granular product that has been incorporated into the topsoil. However, due largely to the relatively low application rate and the nature of the application, no significant exposure risk is expected to occur following a tefluthrin treatment. The only potential source of exposure would result from agricultural workers walking or working on recently treated soil at planting. A restricted-entry interval set at 12 hours will mitigate any risk (both non-cancer and cancer) of exposure for postapplication workers entering an area that has been treated with tefluthrin granules.

Cancer risks are not of concern.

Risks in Residential and Other Non-Occupational Environments

Non-occupational risks are not of concern.

There are currently no residential uses of tefluthrin. Given that homeowners would not be applying the product, a risk assessment for this scenario was not conducted.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Reference doses define levels to which an individual can be exposed over a single day (acute) or lifetime (chronic) and expect no adverse health effects. Generally, dietary exposure from food and water is acceptable if it is less than 100% of the acute reference dose or chronic reference dose (acceptable daily intake). An acceptable daily intake is an estimate of the level of daily exposure to a pesticide residue that, over a lifetime, is believed to have no significant harmful effects.

Human exposure to tefluthrin from residues in treated crops and drinking water, including the most sensitive subpopulation (children one to two years old), was estimated. This aggregate exposure (to tefluthrin from food and drinking water) was less than 76% of the acute reference dose (ARf) and 9.4% of the chronic reference dose.

The lifetime cancer risk was 0.4×10^{-6} and is considered acceptable. A lifetime cancer risk that is less than 1×10^{-6} does not indicate an unacceptable risk for the general population when exposure occurs through pesticide residues in or on food, and to otherwise unintentionally exposed persons. Further information on how the potential cancer risks from pesticides are assessed can be found in Science Policy Notice SPN2000-01, *A Decision Framework for Risk Assessment and Risk Management in the Pest Management Regulatory Agency*.

Based on metabolism data, the residue definition in all commodities is the parent compound, tefluthrin (2,3,5,6-tetrafluoro-4-methylbenzyl (Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate) and its metabolite (cis-3-(2-chloro-3,3,3,trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate). With this residue definition, a maximum residue limit (MRL) of 0.001 ppm was established for milk. An MRL of 0.06 ppm is being proposed for all corn commodities.

Environmental Considerations

What Happens When Tefluthrin Is Introduced Into the Environment?

Tefluthrin poses a potential risk to certain terrestrial and aquatic organisms. Therefore, additional risk-reduction measures need to be observed.

Tefluthrin is an intermediate to high volatility substance. However, it is applied as a granular with subsurface emplacement and volatilization is substantially impeded. In addition, tefluthrin phototransforms rapidly in air and its half life is less than a day. However, tefluthrin is a granular product, which is buried during application and so volatilization of tefluthrin to the air is reduced. It is a moderately persistent substance in the soil and water and it is persistent in sediment. Biotransformation is the dominant mode of transformation in the soil and aquatic systems. Tefluthrin is an insoluble and highly adsorptive material that readily bonds to soil and sediment. It does not leach to groundwater. Its presence in runoff occurs when soil mineral matter containing adsorbed tefluthrin becomes mobile. The log octanol-water partition coefficient is high, which indicates a potential for bioaccumulation. However, tefluthrin does not meet all the criteria under the Toxic Substances Management Policy to be considered as a Track 1 substance.

Tefluthrin was not found to be a risk to earthworms. Bees and beneficial insects are not expected to be exposed to tefluthrin, which is applied as a granular product. Mammals were found to be at risk from inadvertent consumption of tefluthrin granules while foraging for food. Soil mineral matter can be attached to invertebrates and plant material that mammals consume as food sources. Small birds were found to be at risk from consumption of tefluthrin granules as grit. Large non-granivorous birds were found to be at significant risk from inadvertent consumption of granules with food sources. Although tefluthrin is applied as an in-furrow or banded granular application, both field studies and modeling show that runoff events can yield enough tefluthrin to present acute and chronic risks to freshwater fish and amphibians and a risk to freshwater and estuarine/marine invertebrates and estuarine/marine fish. Tefluthrin is not a risk to algae or aquatic plants.

Although tefluthrin presents some risks to small mammals and birds and some aquatic organisms, these risks can be reduced with advisory label statements.

Value Considerations

What is the Value of Tefluthrin?

Tefluthrin is needed for rotation with neonicotinoids for the purpose of resistance management.

For the purpose of resistance management, tefluthrin (a resistance MoA Group 3 insecticide) is needed for rotation with products formulated with active ingredients from a different resistance MoA group.

Measures to Minimize Risk

Registered pesticide product labels include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

Risk-reduction measures are being proposed to address potential risks identified in this assessment. These measures, in addition to those already identified on existing tefluthrin product labels, are designed to further protect human health and the environment. The following additional key risk-reduction measures are being proposed.

Additional Key Risk-Reduction Measures

Human Health

- To protect mixer/loader/applicators: additional protective equipment and restricted-entry intervals are proposed.
- To minimize residues: replant intervals and preharvest intervals are proposed.

Environment

- To reduce the release of tefluthrin into the environment for the protection of terrestrial and aquatic habitats that may contain sensitive species: additional advisory statements to reduce runoff and to protect non-target species are proposed.

What Additional Scientific Information is Being Requested?

The following data are required as a condition of continued registration under section 12 of the *Pest Control Products Act*. The registrants of this active ingredient are required to provide these data or an acceptable scientific rationale within the timeline specified in the decision letter that will be sent to registrants of the technical active ingredients by the PMRA.

Chemistry

DACO 2.13.4	Impurities of human health or environmental concern

Human Health

DACO 4.5.12	Acute neurotoxicity study
DACO 4.5.13	90-day neurotoxicity study
DACO 4.5.14	Developmental neurotoxicity study
DACO 6.2	Poultry metabolism study to confirm goat metabolism
DACO 7.2.2	Validated enforcement methods for all components of the tefluthrin residue definition in animal tissue, milk and eggs

The following data may be required for continued registration depending on the results of the submitted poultry metabolism data for DACO 6.2:

DACO 7.5	Poultry and egg residue data from feeding of treated crops

Next Steps

Before making a re-evaluation decision on tefluthrin, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision, which will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

Other Information

At the time that the re-evaluation decision is made, the PMRA will publish an Evaluation Report on tefluthrin in the context of this re-evaluation decision (based on the Science Evaluation section of this consultation document). In addition, the test data on which the decision is based will also be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

1.0 Introduction

Tefluthrin is a broad spectrum, Resistance Management Mode of Action (MoA) Group 3 insecticide, which acts on the nervous system of insects, and disturbs the function of neurons by interaction with the sodium channel. It works by contact.

Following the re-evaluation announcement for tefluthrin Syngenta Crop Protection Canada Inc., the registrant of the technical grade active ingredient (TGAI) and primary data provider in Canada, indicated that it intended to provide continued support for all uses included on the label of the Commercial Class end-use product.

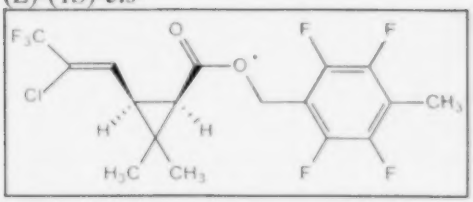
2.0 The Active Substance, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

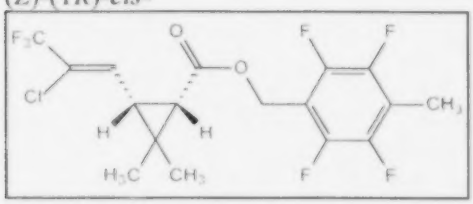
Common name		Tefluthrin
Function		Insecticide
Chemical Family		Pyrethroid
Chemical name		
1	**International Union of Pure and Applied Chemistry (IUPAC)**	2,3,5,6-tetrafluoro-4-methylbenzyl (*Z*)-(1*RS*)-*cis*-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate
2	**Chemical Abstracts Service (CAS)**	(2,3,5,6-tetrafluoro-4-methylphenyl)methyl (1R,3R)-rel-3-[(1Z)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropanecarboxylate
CAS Registry Number		79538-32-2
Molecular Formula		$C_{17}H_{14}ClF_7O_2$

Structural Formula

(*Z*)-(1*S*)-*cis*-



(*Z*)-(1*R*)-*cis*-



Molecular Weight 418.7

Purity of the Technical Grade Active Ingredient 94 % w/w nominal

Registration Number 22616

Identity of relevant impurities of human health or environmental concern:

In 1993, hexachlorobenzene (HCB) was detected in ten batch samples of TGAI at levels ranging from <0.05–0.09ppm. Since then, the supplier has changed the key starting material, which was the likely source of HCB in the TGAI and which could also contribute to the presence of pentachlorobenzene (PCB) and tetrachlorobenzenes (TCBs) in the TGAI. Therefore, new data are required.

Based on the manufacturing process used, no other impurities of human health or environmental concern as identified in the *Canada Gazette*, Part II, Vol. 142, No. 13, SI/2008-67 (2008-06-25), including Toxic Substances Management Policy (TSMP) Track 1 substances, are expected to be present in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 20°C	8.4 mPa
Ultraviolet (UV)/visible spectrum	Not expected to absorb at λ >300 nm
Solubility in water at 20°C	0.02 mg/L
n-Octanol–water partition coefficient (K_{ow}) at 20°C	log K_{ow} = 6.5
Dissociation constant	>9 (hydrolysis prevents measurement)

2.3 Description of Registered Tefluthrin Uses

Appendix I lists all tefluthrin products that are registered under the authority of the *Pest Control Products Act*. Appendix II lists all the uses for which tefluthrin is presently registered. All uses were supported by the registrant at the time of re-evaluation initiation and were therefore considered in the health and environmental risk assessments of tefluthrin.

Uses of tefluthrin belong to the following use-site categories: terrestrial feed crops and terrestrial food crops.

3.0 Impact on Human and Animal Health

3.1 Toxicological Summary

A detailed review of the toxicological database for tefluthrin was conducted. The majority of toxicity studies were conducted between 1984 and 1986 in accordance with the accepted international testing protocols and Good Laboratory Practices at that time. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product. Throughout the toxicological database, the purity of tefluthrin ranged from 90.4% to 96.0%. The results of these toxicological studies revealed consistent target organs, no species differences and similar effect levels for the different exposure scenarios. Based on this information, the different purities of tefluthrin were not expected to impact upon the study conclusions.

Tefluthrin is a synthetic pyrethroid that targets the nervous system by interfering with the sodium channel. In normal neuronal cells, the generation of an action potential by membrane depolarization involves the opening of cell membrane sodium channels and a rapid increase in sodium influx. The closure of sodium channels begins the process of action potential inactivation. The delayed sodium channel closure as a result of tefluthrin exposure thus increases cell membrane excitability and may lead to repetitive firing of sensory nerve endings, which may progress to hyperexcitation of the entire nervous system. Available in vitro data suggest that chloride ion channels and voltage-sensitive calcium channels are not involved in the action of tefluthrin.

Tefluthrin was rapidly absorbed in rats after single or repeat oral dosing with the radiolabel, and mostly concentrated in the liver. Levels of radioactivity were also noted in the fat, ovaries, kidneys and blood. Absorbed tefluthrin was completely metabolized and subsequently excreted via the urine. In comparison, tefluthrin was excreted unchanged via the feces indicating incomplete absorption. In a repeat oral dose metabolism study in rats, excretion via the urine and feces was similar to the excretion profile noted after a single oral dose; however, an increase in the proportion of polar metabolites was noted in the urine after repeat dosing. Excretion was fairly rapid with an extensive proportion of the dosed radioactivity excreted within three days via the feces and the majority of the total dose was eliminated by seven days.

In dogs, a single low oral dose of tefluthrin was rapidly absorbed in a similar pattern to that observed in rats. Absorption of tefluthrin was incomplete with the parent material excreted in the feces. The tissue concentrations of radiolabel peaked shortly after dosing and dropped significantly by day 4. The liver retained the majority of the radiolabeled tefluthrin followed by the fat, kidneys and blood. In the dog, no unchanged tefluthrin was excreted in the bile or urine. The excretion profiles between males and females were similar with the majority of radiolabel eliminated by the fecal route and a minimal amount by the urinary route. This excretion profile of labelled tefluthrin in dogs was similar to that of rats.

Tefluthrin showed high acute toxicity to mice by the oral route of exposure and to rats by the oral, inhalation and dermal routes of exposure. Clinical signs associated with acute exposure to tefluthrin by all routes of exposure in rodents were typical of synthetic pyrethroids and were related to central nervous system excitation. The clinical signs of neurotoxicity noted within one day of exposure included: abnormal/splayed gait, salivation, piloerection, urinary incontinence, upward curvature of spine, tremors and motor incoordination. Additional signs noted in a supplemental acute neurotoxicity study included clonic convulsions, bizarre/stereotypic behavior, hunched body, ataxia and exaggerated hindlimb flexion. In rabbits, tefluthrin was slightly to minimally irritating to the skin and was severely irritating to the eye. In rabbits, signs of parasthesia were also noted and considered to be a common response for exposure to a synthetic pyrethroid. Tefluthrin was not a potential skin sensitizer in guinea pigs.

The major target organ for tefluthrin in repeat-dose toxicological testing was the nervous system with signs typical of pyrethroid toxicity reported in all species examined (mice, rats, rabbits and dogs) by the oral route. At critical effect levels, exposed animals displayed signs of neuromuscular incoordination in conjunction with weight loss and reduced food consumption. Additional confirmatory studies of acute neurotoxicity and 90-day neurotoxicity are being requested. Tefluthrin's effects on organ weights and histopathology (hepatocyte necrosis, minimal foci of hepatocellular alteration, hepatic telangiectasis and spongiosis) suggest that the liver is also a target organ in all examined species, consistent with the distribution studies. Rats exposed to tefluthrin by the dermal route of exposure experienced clinical signs of neurotoxicity. In the dermal study, male rats also experienced alterations in liver weights consistent with the repeat-dose oral studies. Repeat-dose inhalation studies were not available. No clear gender sensitivities were seen in short-term or chronic repeat-dose toxicity studies. There is limited evidence of increased toxicity with increased duration of exposure in rats, based on adverse effects on body weight at lower doses in longer-term studies.

In two-year chronic toxicity/carcinogenicity studies in mice and rats, clinical signs of neurotoxicity were noted, consistent with the short-term, repeat-dose toxicity studies. In both males and females, the liver was targeted by tefluthrin resulting in alterations of organ weights and histopathology. Effects on organ weights and histopathology were also noted in the spleen and testes of male mice and the uterus and ovaries of female mice. In female mice, a treatment-related increased incidence of benign type A liver nodules was noted at the high-dose; however, there was no evidence of progression to a malignant lesion. High-dose female rats also experienced slight increases in the incidence of pituitary cysts, cystic ovaries, uterine luminal distension and cervical fibromuscular hyperplasia. While these lesions appear to be related to the endocrine and reproductive systems, no hormonal data were provided to explain a possible MoA.

Neoplastic findings in high-dose female rats included an increased incidence of adenocarcinoma of the uterus. Even though the incidence of this lesion in high-dose female rats was not statistically significant as compared to the control values, the dose-response curve was shallow and the incidence at the high-dose was just outside the historical control range provided by the registrant. Based on the study results, there is evidence of tumourigenicity in female mice and carcinogenicity in female rats. In both male mice and rats exposed to tefluthrin, there is no evidence of carcinogenicity.

Assessments of mutagenic potential were performed for tefluthrin in a variety of bacterial and mammalian in vitro and in vivo genotoxicity studies. Negative results were obtained in an in vitro unscheduled DNA synthesis assay, an Ames test and a mouse lymphoma mutagenesis assay. Negative results were also obtained in in vivo studies such as a micronucleus assay, a dominant lethal study and a cytogenicity study under the test conditions. Tefluthrin was not mutagenic in these in vitro and in vivo genotoxicity studies.

In the two-generation rat reproduction study, parental toxicity was indicated by reduced body weight, food consumption and an excitation in the central nervous system. There was evidence of a treatment-related effect on reproductive performance with decreased litter size at birth, total litter weight at birth and shorter median pre-coital intervals. High-dose pups had decreased body weight and body weight gain in comparison to control pups. An enhancement of clinical signs of neurotoxicity was noted with multigenerational exposure to tefluthrin as evidenced by an increased incidence of shaking in the mid-dose second generation pups. An increased incidence of shaking along with abnormal and splayed gait was also noted at the high-dose level in the second generation pups. Based on evidence of neurotoxicity in the offspring in the absence of parental toxicity, there is quantitative sensitivity of the young. A developmental neurotoxicity study is requested.

In an oral teratogenicity study in rats, maternal toxicity was noted in the form of subdued behaviour along with decreased body weight gain and food consumption. Toxicity in the tefluthrin-exposed offspring was noted in the form of skeletal variations (25 pre-sacral vertebrae). In a developmental toxicity study conducted with rabbits administered tefluthrin by gavage, clinical signs of neurotoxicity were noted in all treated dams. With increasing doses, the number of dams affected and the severity of neurotoxic effects occurred with an increased frequency. The tefluthrin exposed offspring experienced a dose-related increase in the number of skeletal variations (extra 13^{th} ribs and 27^{th} pre-sacral vertebrae). The skeletal variations were noted in the presence of maternal toxicity for both rats and rabbits and neither species showed evidence of teratogenicity.

In a supplemental acute delayed neurotoxicity study in hens, tefluthrin produced an acute neuropathological response. Hens exposed to tefluthrin experienced decreased body weight gain and food consumption, subdued behaviour, unsteadiness, stumbling, trembling, wing flapping, inability to stand or walk, lying on one side and eyes closed with head and neck rotating shortly after dosing. The majority of survivors had recovered by days five and six. There was no indication that tefluthrin induced acute delayed neurotoxicity. Nerve conduction velocity measurements in rats receiving repeated oral doses of tefluthrin suggest a transient effect on sensory nerves.

Subjective facial sensation (SFS)—a transient tingling, burning, itching or numb feeling of the skin (usually of the face)—is commonly noted in humans exposed to synthetic pyrethroids. In the case of tefluthrin, studies in humans have demonstrated a mild to moderate SFS after using a tefluthrin formulation with the symptoms disappearing in less than eight hours.

Results of the acute and chronic tests conducted on laboratory animals with tefluthrin technical, along with the toxicology endpoints for use in the human health risk assessment, are summarized in Appendix III, Table 1 and Table 2.

3.1.1 *Pest Control Products Act* Hazard Characterization

For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor to threshold effects. This factor should take into account completeness of the data with respect to the exposure of, and toxicity to, infants and children and potential pre- and postnatal toxicity. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database as it pertains to the exposure of and toxicity to infants and children, numerous studies were available for tefluthrin, with the exception of acute and short-term neurotoxicity studies and a developmental neurotoxicity study. These studies represent a significant data gap for a compound with an established neurotoxic MoA. Although an acute neurotoxicity study was available, the study was considered supplemental due to limitations resulting from the study intent and design. The remaining studies comprising the tefluthrin database were of high quality and included a developmental toxicity study in rats, a developmental toxicity study in rabbits and a multi-generation reproduction study in rats.

With respect to potential pre-and postnatal toxicity, developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of fetuses to in utero exposure. The two-generation reproductive toxicity study in rats revealed clinical signs of neurotoxicity (shaking and abnormal/splayed gait) in both the parents and offspring, which was progressive with successive generations. Of potential concern was the occurrence of neurotoxic effects in the offspring in the absence of maternal toxicity. The presence of quantitative sensitivity of the young in the two-generation rat reproduction study, particularly relating to neurotoxicity, reinforces the need for a developmental neurotoxicity study.

3.2 Occupational and Non-Occupational Risk Assessment

Occupational and non-occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating uncertainty factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects. However, MOEs less than the target MOE require measures to mitigate (reduce) risk. Dermal and inhalation exposures were combined because of a common toxicity endpoint and because dermal and inhalation exposures may occur simultaneously. A combined MOE was used to combine short- to intermediate-term dermal and

inhalation risk estimates since the dermal and inhalation target MOEs are identical. A combined MOE ≥1000 does not exceed the PMRA's level of concern for short- or intermediate-term risk assessments.

3.2.1 Toxicology Endpoint Selection for Occupational and Residential Risk Assessment

3.2.1.1 Short- and Intermediate-term Dermal Risk Assessment

For occupational short- and intermediate-term dermal assessment relative to the use pattern (1–30 days and 1 month–several months, respectively), the dermal no observable adverse effect level (NOAEL) of 1 mg/kg bw/day from the 21-day dermal toxicity study in Wistar rats was selected based on signs of neurotoxicity noted at the next dose level of 5 mg/kg bw/day. The target MOE selected when using this study is 1000, thus accounting for standard uncertainty factors of 10-fold for interspecies extrapolation, and 10-fold for intraspecies variability. An additional uncertainty factor of 10-fold has also been applied to account for data deficiencies, namely the absence of a short-term neurotoxicity study and a developmental neurotoxicity study. This target MOE provides adequate margins to the other endpoints noted in the database.

3.2.1.2 Short- and Intermediate-term Inhalation Risk Assessment

Since there are no repeat-dose inhalation studies available for inhalation risk assessment, it is assumed that absorption via inhalation exposure is equivalent to that following oral exposure.

For occupational short- (1–30 days) and intermediate-term (1 month–several months) inhalation assessment relative to the use pattern, the NOAEL of 0.5 mg/kg bw/day from a 12-month oral (by capsule) study in beagle dogs was selected. At the next dosage level of 2 mg/kg bw/day, signs of neurotoxicity (ataxia, unsteady gait, body tremors and vomiting) along with decreased body weight gain were noted in both males and females. The target MOE is 1000 thus accounting for the standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability. An additional uncertainty factor of 10-fold has also been applied to account for data deficiencies, namely the absence of a short-term neurotoxicity study and a developmental neurotoxicity study. This MOE is protective of other endpoints noted in the database.

3.2.1.3 Endpoint Selection for Aggregate Assessment

Aggregate exposure to tefluthrin may be comprised of food and drinking water exposures; there are no residential uses for tefluthrin. The most relevant studies are those selected for the ARfD and acceptable daily intake (ADI) for acute and repeated exposure scenarios, respectively.

3.2.1.4 Cancer Potency Factor

In the absence of MoA data to support a threshold approach to the cancer risk assessment, a linear low dose extrapolation approach (Q_1^*) was used for tefluthrin. Unit risks for tefluthrin, denoted by Q_1^* (representing the upper 95% confidence limit on the slope of the dose-response curve in the low-dose region), were calculated on the basis of the bioassay data from the two

year chronic toxicity/carcinogenicity studies in the mouse and the rat. An adjusted Q_1^* value of 2.43×10^{-2} (mg/kg bw/day)$^{-1}$ was derived in females for the increased incidence of hepatic type A benign nodules from the two year chronic toxicity/carcinogenicity study in mice. An adjusted Q_1^* value of 3.07×10^{-2} (mg/kg bw/day)$^{-1}$ was calculated from the two-year chronic toxicity/carcinogenicity study in rats based on the increased incidence of adenocarcinoma of the uterus in females. For the cancer risk assessment of tefluthrin, the more conservative adjusted Q_1^* value of 3.07×10^{-2} (mg/kg bw/day)$^{-1}$ from the two year chronic toxicity/carcinogenicity study in rats was selected.

3.2.1.5 Dermal Absorption

A dermal absorption factor is not applicable for the risk assessment since the toxicological endpoint for dermal exposure was based on a dermal study.

3.2.2 Occupational Exposure and Risk Assessment

Workers can be exposed to tefluthrin through mixing, loading or applying the pesticide, and, to a lesser extent, when entering a treated site to conduct activities such as scouting.

3.2.2.1 Mixer, Loader and Applicator Exposure and Risk Assessment

There are potential exposures to mixers, loaders, and applicators. The following supported uses were assessed:

A. Mixing and loading granules:

Open mixing and loading with maximum personal protective equipment (PPE): Chemical resistant coveralls over a single layer (long sleeved shirt, long pants, socks plus shoes) with chemical resistant gloves.

Open mixing and loading with maximum PPE and a respirator: Chemical resistant coveralls over a single layer (long sleeved shirt, long pants, socks plus shoes) with chemical resistant gloves and a suitable respirator.

B. Applying granules by tractor drawn broadcast spreader:

Maximum PPE: Chemical resistant coveralls over a single layer (long sleeved shirt, long pants, socks plus shoes). Chemical resistant gloves for all tasks outside of the closed cab.

Occupational non-cancer and cancer risk estimates associated with applying, mixing and loading for agricultural uses meet the targets provided engineering controls and/or PPE are used as summarized in Appendix IV, Table 1. Table 1 and Table 2 of Appendix IV summarize the calculated MOEs and cancer risks for mixers, loaders and applicators.

Although the current use of tefluthrin marginally fails to meet the target combined MOE of 1000, there are built in conservatisms in the risk assessment, such as the use of default protection factors and maximum rates of application. These conservatisms may have resulted in an overestimation of exposure or an underestimation of afforded protection. In addition, when

considered separately, the calculated dermal and inhalation MOEs each met their targets of 1000. Since the calculated combined MOE sufficiently approaches the target, the risk of exposure for mixer/loader/applicators is not of concern, provided all the mitigation measures described herein are applied.

No acceptable chemical-specific handler exposure data were submitted for tefluthrin; therefore, dermal and inhalation exposures were estimated using data from the Pesticide Handlers Exposure Database (PHED), Version 1.1. The PHED is a compilation of generic mixer/loader and applicator passive dosimetry data with associated software that facilitates the generation of scenario-specific exposure estimates based on formulation type, application equipment, mix/load systems and level of PPE.

In most cases, PHED did not contain appropriate data sets to estimate exposure to workers wearing chemical-resistant coveralls or a respirator. This was estimated by incorporating a 90% clothing protection factor for chemical resistant coveralls and 90% protection factor for a respirator into the inhalation unit exposure data. Inhalation exposures were based on light inhalation rates (17 litres per minute).

Mixer/loader/applicator exposure estimates are based on the best available data at this time. The assessment might be refined with exposure data representative of modern application equipment and engineering controls. Biological monitoring data could also further refine the assessment.

3.2.2.2 Postapplication Worker Exposure and Risk Assessment

Postapplication exposure typically includes activities such as scouting, pruning, harvesting, training, irrigation, and transplanting. Due to the limited number of applications per year (one per year) exposure to tefluthrin is likely to be short-term in duration. Dermal exposure to workers re-entering treated areas is typically calculated using dislodgeable foliar residue values, which are crop specific, and transfer coefficients, which are activity specific.

The PMRA is primarily concerned with the potential for dermal exposure for workers performing postapplication activities in crops treated with a foliar spray. The only tefluthrin product registered in Canada is a granular formulation, which is incorporated into the topsoil. It is applied at corn planting only, thereby precluding most of the typical re-entry activities, such as harvesting, that may result in occupational postapplication exposure. Since tefluthrin is not applied to foliage, dislodgeable foliar residue values are not applicable, and the risk of residue transfer from corn plants to agricultural workers is negligible.

No data exist to adequately assess postapplication exposure to tefluthrin from areas treated with a granular product. However, due largely to the relatively low application rate (0.15 kg a.i./ha) and the nature of the application, no significant exposure risk is expected to occur following a tefluthrin treatment. The only potential source of exposure would result from agricultural workers walking or working on recently treated soil at planting. A minimum restricted-entry interval set at 12 hours will mitigate any risk (both non-cancer and cancer) of exposure for postapplication workers entering an area that has been treated with tefluthrin granules.

The assessments could be refined and uncertainties reduced with the following data:

- Enhanced information on the tefluthrin use pattern, including typical rates
- Survey information on critical worker activities that typically take place for each crop during the use season, and the timing of these activities with respect to crop growth and applications of tefluthrin
- Passive dosimetry or biological monitoring data

Postapplication cancer risks for workers performing postapplication activities are not of concern.

3.2.3 Non-Occupational and Residential Exposure and Risk Assessment

Non-occupational risk assessment is concerned with estimating risks to the general population, including children, during or after pesticide application in and around the home. Given that there are no domestic products for tefluthrin nor are there any residential uses, a non-occupational assessment was not conducted.

3.3 Dietary Risk Assessment

In a dietary exposure assessment, the PMRA determines how much pesticide residue, including residues in milk and meat, may be ingested with the daily diet. Exposure to tefluthrin from potentially treated imports is also included in the assessment. These dietary assessments are age specific and incorporate the different eating habits of the population at various stages of life. For example, the assessments take into account differences in children's eating patterns, such as food preferences and the greater consumption of food relative to their body weight when compared to adults. Dietary risk is then determined by the combination of the exposure and the toxicity assessments. High toxicity may not indicate high risk, if the exposure is low. Similarly, there may be risk from a pesticide with low toxicity if the exposure is high.

The PMRA considers limiting use of a pesticide when risk exceeds 100% of the reference dose. The PMRA's Science Policy Note SPN2003-03, *Assessing Exposure from Pesticides in Food, A User's Guide*, presents detailed acute and chronic risk assessments procedures.

Residue estimates used in the dietary risk assessment may be conservatively based on the MRL or the field trial data representing the residues that may remain on food after treatment at the maximum label rate. Surveillance data representative of the national food supply may also be used to derive a more accurate estimate of residues that may remain on food when it is purchased. These include the Canadian Food Inspection Agency's National Chemical Residue Monitoring Program and the United States Department of Agriculture Pesticide Data Program.

Acute and chronic non-cancer and cancer dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

The dietary risk assessment considered potential residues in animal commodities by incorporating anticipated residue estimates, which were based on data from animal metabolism studies and the maximum dietary burden.

For more information on dietary risk estimates or residue chemistry information used in the dietary assessment, see Appendix V and VI.

3.3.1 Determination of Acute Reference Dose

To estimate acute dietary risk (1 day), an oral (gavage) teratogenicity study in the Wistar rat was selected for risk assessment purposes, with the assumption that the neurotoxic effects in this study may arise from a single exposure. A NOAEL of 1 mg/kg bw/day was selected based on maternal toxicity in the form of decreased food consumption, body weight gain and subdued behaviour at the next dosage level of 3 mg/kg bw/day. The selection of this study and NOAEL was supported by the observations noted in dogs shortly after dosing (two to six hours post-dosing) with ≥3 mg/kg bw/day in a six week range-finding study. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. An additional uncertainty factor of 10-fold has also been applied to account for data deficiencies, namely the absence of an acceptable acute neurotoxicity study and a developmental neurotoxicity study. The *Pest Control Products Act* factor can be reduced to onefold as residual concerns have been subsumed through the application of the data deficiency uncertainty factor.

$$\text{ARfD} = \frac{\text{1 mg/kg bw/day}}{\text{1,000}} = 0.001 \text{ mg/kg bw}$$

3.3.2 Acute Dietary Exposure and Risk Assessment

Acute dietary risk is calculated considering the highest ingestion of tefluthrin that would be likely to occur on any one day, using food and drinking water consumption data and the estimated residue values on those commodities. Acute dietary aggregate (food and water) risk was assessed using refined probabilistic methods at 99.9th percentile of this distribution and was compared to the ARfD, which is the dose at which an individual could be exposed on any given day and expect no adverse health effects. When the expected intake of residues is less than the ARfD, then acute dietary exposure is considered to be acceptable.

The acute potential daily intake of tefluthrin from food and water accounted for less than 76% (99.9th percentile) of the ARfD for all subpopulations and is, therefore, not of concern.

3.3.3 Determination of Acceptable Daily Intake

The major target organ for tefluthrin in all evaluated species (mice, rats, rabbits and dogs) was the nervous system with signs typical of pyrethroid toxicity consistently noted throughout the database. To estimate dietary risk from repeat exposure, the most suitable study was a 12-month oral (by capsule) study in beagle dogs. A NOAEL of 0.5 mg/kg bw/day was established based on signs of neurotoxicity, including ataxia, unsteady gait, body tremors and vomiting along with decreased body weight gain in both males and females at the next dosage level of

2 mg/kg bw/day. Standard uncertainty factors of 10-fold for interspecies extrapolation and 10-fold for intraspecies variability were applied. An additional uncertainty factor of 10-fold has also been applied to account for data deficiencies, namely the absence of a short-term neurotoxicity study and a developmental neurotoxicity study. The *Pest Control Products Act* factor can be reduced to 1-fold as residual concerns have been subsumed through the application of the data deficiency uncertainty factor.

$$\text{ADI} = \frac{0.5 \text{ mg/kg bw/day}}{1{,}000} = 0.0005 \text{ mg/kg bw/day}$$

This ADI provides a margin of >1,760 to the lowest NOAELs for developmental toxicity, >585 for parental toxicity and >440 for offspring effects. It is thus considered protective of all populations including pregnant women, infants and children.

3.3.4 Chronic Non-Cancer Dietary Exposure and Risk Assessment

The chronic dietary risk was calculated by using the average consumption of different foods and drinking water and the estimated residue values on those commodities. This expected intake of residues was then compared to the ADI. When the expected intake of residues is less than the ADI, then chronic dietary exposure is considered to be acceptable.

The chronic potential daily intake of tefluthrin from food and water accounted for <9.4% of the ADI for all subpopulations and is, therefore, not of concern.

3.3.5 Carcinogenic Dietary Exposure and Risk Assessment

The cancer risk from dietary exposure (food and water) to tefluthrin was 0.4×10^{-6} and is not of concern. A lifetime cancer risk that is below 1×10^{-6} does not indicate an unacceptable risk for the general population when exposure occurs through pesticide residues in or on food, and to otherwise unintentionally exposed persons.

3.4 Exposure from Drinking Water

3.4.1 Concentrations in Drinking Water

Estimated environmental concentrations (EECs) of tefluthrin in potential drinking water sources (groundwater and surface water) were estimated using computer simulation models. These models predicted that no residues will reach groundwater. For residues in reservoirs, the acute and chronic exposure concentrations predicted by PRZM/EXAMS were estimated to be 0.14 and 0.01 µg a.i./L, respectively. For residues in dugouts, the acute and chronic exposure concentrations predicted by PRZM/EXAMS were estimated to be 0.15 and 0.04 µg a.i./L, respectively.

3.4.2 Drinking Water Exposure and Risk Assessment

Drinking water exposure was considered in the acute and chronic non-cancer and cancer dietary assessments as both food and water consumption data and residue estimates were included in the assessments. For the acute assessment, residues in drinking water were based on the highest daily EEC (0.15 µg a.i/L). In the chronic non-cancer and cancer assessment, residues in drinking water were based on the highest yearly EEC (0.04 µg a.i/L). As noted in Section 3.3, the drinking water estimates were incorporated directly in the dietary exposure assessment

3.5 Aggregate Risk Assessment

Aggregate exposure is the total exposure to a single pesticide that may occur from food, drinking water and residential sources as well as from all known or plausible exposure routes (oral, dermal and inhalation). As tefluthrin is not registered for residential uses, the aggregate risk assessment considered exposure from food and drinking only. As noted in 3.3, the acute, chronic and cancer aggregate risk assessment were not of concern.

3.6 Incident Reports

Starting 26 April 2007, registrants are required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Incidents are classified into six major categories including effects on humans, effects on domestic animals and packaging failure. Incidents are further classified by severity, in the case of humans for instance, from minor effects such as skin rash, headache, etc., to major effects such as reproductive or developmental effects, life-threatening conditions or death.

The PMRA will examine incident reports and, where there are reasonable grounds to suggest that the health and environmental risks of the pesticide are no longer acceptable, appropriate measures will be taken, ranging from minor label changes to discontinuation of the product.

There was one American incident report related to human health submitted to the PMRA for tefluthrin as of 1 December 2008. The incident involved an apparent accident with a liquid formulation of tefluthrin. However, cause of death was not confirmed to be associated with exposure to the product. The latest information received by the PMRA indicates that the death was likely the result of a cardiac incident. Since there are no liquid tefluthrin products registered in Canada, this type of incidental exposure is unlikely to occur.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Tefluthrin is an insoluble, intermediate to high volatility substance (vapour pressure of 8.4 mPa at 20°C), which is rapidly lost from water and moist soil surfaces (Henry's Law constant (1/H) is 10.4 (K= 234 Pa m^3/mol at 20°C). However, it is applied as a granular formulation with subsurface emplacement and so volatilization is only a minor route of dissipation. It does not dissociate in water. The log K_{ow} of tefluthrin is very high (6.4) and indicates a high potential for bioaccumulation.

Abiotic processes such as hydrolysis and photolysis are not important routes of transformation of tefluthrin in soil or water. However, tefluthrin phototransforms rapidly in air and its half life is 0.94 days. Biotransformation is the main route of transformation of tefluthrin in soils and the aquatic environment. In soil, it is moderately persistent, with maximum dissipation time to 50% (DT_{50}) and dissipation time to 90% (DT_{90}) values of 63 days and 163 days, respectively, and in water-sediment systems (whole system) of 146 days and 190 days, respectively. No major transformation products (>10 % of the applied active) were detected in the aerobic soil biotransformation studies. In soil, the tefluthrin molecule undergoes mineralization to CO_2 with no major transformation products. In aquatic systems the only major transformation product detected was compound Ia in water (maximum of 22% of applied active). In the sediment alone, tefluthrin is persistent, with a maximum DT_{50} value of 204 days.

Since it is buried as an in-furrow or banded granular emplacement, tefluthrin generally only reaches water bodies after more extreme rainfall events where there is significant erosion and transport of soil. If tefluthrin bound to sediment does reach water bodies, aerobic biotransformation is expected to be the major route of transformation. There are no data available on the aquatic biotransformation of tefluthrin under anaerobic conditions.

Tefluthrin is a highly adsorptive substance and, therefore, it is immobile in soil (organic carbon partition coefficient (K_{oc}) values 24,200–267,000) and is not expected to leach to groundwater. Aged soil column leaching studies confirm that tefluthrin and its transformation products are not mobile in soil and do not leach below 5 cm.

The American and Canadian field studies of granular applied tefluthrin dissipation in soils indicate that it is moderately persistent, with maximum dissipation time to 50% (DT_{50}) and dissipation time to 90% (DT_{90}) values of 165 days and 495 days, respectively. This indicates the possibility of some carryover into the next year. Tefluthrin was not detected in any of these studies at depths greater than 10 cm and no transformation products were detected at concentrations exceeding 1% of applied tefluthrin at depths greater than 20 cm.

Studies of tefluthrin in runoff from treated sites to small ponds and collection flumes, following simulated rainfall (irrigation) and natural rainfall, indicate that buried granular applications are capable of generating runoff of tefluthrin bound to soil particles. T-banded applications of tefluthrin (Force 3G) resulted in up to 0.9% of applied tefluthrin in runoff. Another study of natural rainfall events, found up to 3% of applied tefluthrin occurred in runoff after intense rainfall events. However, for most events the amount in runoff was <0.5% of the amount applied.

4.2 Effects on Non-Target Species

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. EECs are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (in other words, protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, direct application at a maximum cumulative application rate) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC = 1). If the screening level is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as drift to non-target habitats) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Effects on Terrestrial Organisms

As tefluthrin is a granular insecticide and is buried, bees and beneficial insects are not expected to be exposed to it and would not be at risk. Data were not available on its toxicity to plants. Since tefluthrin is an insecticide, it is not expected to pose a risk to plants. A risk assessment of tefluthrin to the remaining terrestrial organisms was based upon an evaluation of toxicity data on tefluthrin to earthworms (acute), birds (acute oral, and reproductive (chronic)), mammals (acute oral, and reproductive). A summary of terrestrial toxicity data for tefluthrin is presented in Appendix VII, Table 3. Results of the screening level risk assessment are shown in Appendix VII, Tables 4–8.

The screening level risk assessment indicates that tefluthrin exceeds the acute and the reproductive LOC for both birds and mammals by a wide margin. The RQ values based on acute oral risk to birds ranged from 287 for a 20 g bird to 65 for a 1000 g bird. Assessment of the reproductive risk to birds also showed an exceedance of the LOC with the RQ values ranging from 5429 for a 20 g bird to 1235 for a 1000 g bird. The RQ values based on acute oral risk to small mammals ranged from 2019 for a 15 g mammal to 946 for a 1000 g mammal. Assessment of the reproductive risk to small mammals also showed an exceedance of the LOC with the RQ values ranging from 5,855 for a 15 g mammal to 2,749 for a 1000 g mammal.

A refined on-field risk assessment was carried out for birds and mammals assuming 15% of granules remain exposed at the surface (Appendix VII, Tables 9–12). The refined risk assessment took into consideration the maximum number of granules consumed per day by birds, which deliberately consume grit to aid in their digestion (for example, granivores and omnivores) and have distinct grit preferences. It also considered birds that consume grit inadvertently (for example, herbivores) while foraging for food and can consume large quantities of very fine textured grit. The refined assessment indicated that the acute risk to birds was negligible. The risk quotients were less than the LOC for 20 g, 100 g, and 1000 g birds, the latter for both granivorous birds that selectively choose their grit, and nongranivorous birds. The reproductive (chronic) LOC was not exceeded for 100 g birds. However, the chronic LOC was exceeded for 20 g birds (RQ = 4.3). The LOC was also exceeded for 1000 g nongranivorous birds (RQ = 299) due to their tendency to consume large quantities of granules indiscriminately while foraging for food. However, this assumes that the birds are foraging exclusively on treated areas for several weeks during the reproductive period.

Small mammals inadvertently consume soil mineral matter while foraging for food and so mammals can be exposed to spilled tefluthrin granules at row ends or granules near the surface (for example, banded applications). For shrews and voles the maximum soil mineral content is 2.4% of the diet and for the rabbit up to 6.3%. The refined risk assessment took this into consideration and showed that there was a potential risk to mammals foraging for food. For mammals the refined risk assessment indicated that both the acute LOC (RQ 16–23) and chronic LOC (RQ 489–683) were exceeded for the 15 g, 35 g and 1000 g mammals.

4.2.2 Effects on Aquatic Organisms

Tefluthrin is acutely toxic to rainbow trout with a lethal concentration on 50% of the population (LC_{50}) of 0.06 µg a.i./L. The acute effective concentration on 50% of the population (EC_{50}) for the freshwater invertebrate *Daphnia magna* is 0.07 µg a.i./L. A life cycle study with fathead minnow, indicated a no observed effect concentration (NOEC) on survival of the F_1 generation of 0.00397 µg a.i./L. For the invertebrates, the NOEC for *Daphnia magna* was 0.00792 µg a.i./L based on the total number of live young produced. The tefluthrin toxicity to the green algae *Pseudokirchnerialla subcapitata* was EC_{50} of >1.05 mg a.i./L (Appendix VII, Table 3).

The screening level aquatic assessment (Appendix VII, Tables 13–21) indicates that tefluthrin exceeds the LOC for aquatic invertebrates, fish and amphibians by very large margins. For freshwater invertebrates, the LOC values for acute and chronic risk were exceeded (acute RQ 403–537, chronic RQ 1780–2374) and similarly for the acute risk to estuarine/marine invertebrates (RQ 532–709). Chronic toxicity data for estuarine/marine invertebrates were not available. For freshwater fish, the LOC values for acute and chronic risk were exceeded (acute RQ 2350 -3133, chronic RQ 3552–4735) and similarly for the acute risk to estuarine/marine fish (RQ 1084–1446). Chronic toxicity data for estuarine/marine fish were not available. Tefluthrin was also identified as a risk to amphibians (acute RQ 12500–16667, chronic RQ 20270–27027). Tefluthrin does not pose a risk to algae or aquatic plants at the screening level.

A refined risk assessment was carried out using runoff modeling data from corn crops treated with tefluthrin in various regions of Canada where it is used. The modeling scenarios were located in Ontario, Quebec, B.C., Manitoba and Prince Edward Island (P.E.I.), with Manitoba representing the entire prairie region, and P.E.I. representing the Atlantic region. The results of the refined aquatic risk assessment are shown in Appendix VII, Tables 22–29. These indicate that tefluthrin in runoff posed a negligible risk to freshwater invertebrates (acute RQ's 0.2 –0.9) and only exceeded the LOC for chronic effects in regard to the P.E.I. corn scenario (chronic RQ 1.6). There was acute risk to estuarine/marine invertebrates only from runoff from the P.E.I. corn scenario (RQ 1.1). Tefluthrin in runoff was an acute risk to freshwater fish (RQ values 1.3–5.0). There was a potential chronic risk to freshwater and estuarine/marine fish only from runoff from the P.E.I. corn scenario (RQ 1.8 for freshwater and RQ 2.3 estuarine/marine). Tefluthrin was an acute risk to amphibians from runoff (RQ 5.5–22). The exceedance of the LOC for chronic effects in amphibians only occurred from runoff from the P.E.I. corn scenario (RQ 2.2).

In conclusion, runoff from corn treated with granular tefluthrin does pose a potential risk to aquatic life, in particular amphibians and freshwater fish.

5.0 Value

There are few registered alternative active ingredients to tefluthrin for the control of wireworms, seedcorn maggot, northern corn rootworm and western corn rootworm. Registered alternative active ingredients are available for the control of black cutworm.

For the purpose of resistance management, tefluthrin (a resistance MoA Group 3 insecticide) is needed for rotation with products formulated with active ingredients from a different resistance MoA group.

For the control of wireworms, neonicotinoids (MoA Group 4 insecticides) are the only registered alternative active ingredients to tefluthrin (MoA Group 3).

For the control of seed corn maggot and western corn rootworm, the registered alternative active ingredients to tefluthrin other than the neonicotinoids (clothianidin and thiamethoxam) are organophosphates (MoA group 1B), which are currently under re-evaluation.

For northern corn rootworm control, the alternative active ingredients to tefluthrin other than the neonicotinoids (clothianidin and thiamethoxam) are organophosphates or carbamates (MoA Group 1A) which are currently under re-evaluation. Additionally, some alternatives are only registered for post-emergent use on the crop, thereby limiting control to the adult beetles.

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The TSMP is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy—persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

During the review process, tefluthrin and its transformation products were assessed in accordance with the PMRA Regulatory Directive DIR99-03[6] and evaluated against the Track 1 criteria. The PMRA has reached the following conclusions:

- Tefluthrin does not meet the Track 1 criteria for persistence, and is not considered a Track 1 substance. See Table 1 in Appendix VII for comparison with Track 1 criteria.

- There are several major transformation products of tefluthrin. There are insufficient data available on the transformation products to determine whether they meet the Track 1 criteria or not.

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[6] DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*.

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical are compared against the list identified in the *Canada Gazette*, Part II Volume 139, Number 24, pages 2641-2643: *List of Pest Control Product Formulants and Contaminants of Health of Environmental Concern.* The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including DIR99-03 and Regulatory Directive DIR2006-02[8], and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade tefluthrin (Registration Number 22616) has been shown to be contaminated with the contaminant HCB, which has been identified in the federal government's TSMP (1995) as a Track 1 substance. The PMRA is continuing its efforts to implement the Agency's strategy to manage Track 1 contaminants in pest control products on an ongoing basis as per Regulatory Directive DIR99-03. The purpose is to prevent or minimize releases, with the ultimate goal of virtual elimination.

- Information on the levels of HCB in tefluthrin was generated in 1993. For PMRA to evaluate current progress being made towards the virtual elimination of Track 1 substances, recent information on the current levels of HCB, PCB, and TCBs is required.

- The use of formulants in registered pest control products identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[9] is assessed on an ongoing basis through PMRA formulant initiatives and DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for tefluthrin is adequate to define the majority of toxic effects that may result from human exposure to tefluthrin. There was no evidence that tefluthrin was genotoxic or teratogenic. In female rats, there was evidence of carcinogenicity in the form of uterine adenocarcinomas. Benign liver tumours were observed in female mice. Tefluthrin did not

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7 NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act.*

8 DIR2006-02, *PMRA Formulants Policy.*

9 *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions* and *Part 3 Contaminants of Health or Environmental Concern.*

cause cancer in male mice or rats. The major target organ for tefluthrin in repeat-dose toxicological testing was the nervous system with signs typical of pyrethroid toxicity reported in all species examined by the oral route and in rats examined by the dermal route. Tefluthrin's effect on organ weights and histopathology suggest that the liver is also a target organ in all examined species. When tefluthrin was given to pregnant animals, an enhancement of clinical signs of neurotoxicity was noted with multigenerational exposure. Based on evidence of neurotoxicity in the offspring in the absence of parental toxicity, there is a sensitivity of the young animal to tefluthrin. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

7.1.1 Occupational Risk

Non-cancer and cancer risk estimates associated with applying, mixing and loading activities for the agricultural label uses are not of concern, provided engineering controls or personal protective equipment are used. Postapplication risks for workers were not of concern when the proposed mitigation measures are applied.

Postapplication cancer risk was not of concern.

7.1.2 Dietary Risk from Food

Acute, chronic non-cancer and cancer risk estimates associated with exposure of tefluthrin from food are not of concern.

7.1.3 Dietary Risk from Drinking Water

Acute, chronic non-cancer and cancer risk estimates associated with exposure of tefluthrin from water are not of concern.

7.1.4 Non-Occupational Risk

Given that there are no residential uses of tefluthrin, a risk assessment for this scenario was not conducted.

7.1.5 Aggregate Risk

The aggregate risk from food and drinking water are not of concern.

7.2 Environmental Risk

The use of granular tefluthrin (Force 3G) on corn does present a potential risk to aquatic organisms, in particular amphibians and freshwater fish. The risk to aquatic life may be reduced through the use of vegetative filter strips to reduce soil transport in runoff to water bodies, as well as advisory label statements. Granular tefluthrin poses a potential risk to small mammals and to some birds, in particular larger birds (1000 g body weight), which do not selectively

choose their grit. This is due to their tendency to inadvertently consume soil mineral matter while foraging for food. However, this assumes that these birds are foraging exclusively on treated areas. Advisory label statements are specified to inform the user of this hazard.

7.3 Value

Tefluthrin has value for pest control in corn and is required for rotation with neonicotinoids for the purpose of resistance management.

8.0 Proposed Regulatory Decision

The PMRA is proposing that tefluthrin is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. As a condition of continued registration of tefluthrin, the new risk-reduction measures must be included on the labels of all products and confirmatory data are required.

8.1 Proposed Regulatory Actions

8.1.1 Proposed Regulatory Action Related to Human Health

For agricultural uses, the PMRA has determined that the dietary and drinking water risks and the worker risks during mixing, loading and application and during postapplication activities are not of concern, provided that the mitigation measures listed in this section are implemented.

Appendix VIII summarizes the use limitations and minimum PPE for the commercial class products containing tefluthrin resulting from this re-evaluation.

8.1.1.1 Residue Definition for Risk Assessment and Enforcement

Based on plant and animal metabolism studies, the residue definition in all commodities is currently expressed as the combined residue of the parent compound, tefluthrin (2,3,5,6-tetrafluoro-4-methylbenzyl (*Z*)-(1*RS*)-*cis*-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate) including metabolites containing the (cis-3-(Z-2-chloro-3,3,3,trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate) moiety.

8.1.1.2 Maximum Residue Limits for Tefluthrin in Food

In general, when the re-evaluation of a pesticide has been completed, the PMRA intends to update Canadian MRLs remove those that are no longer supported. The PMRA recognizes, however, that interested parties may want to retain an MRL in the absence of a Canadian registration to allow legal importation of treated commodities into Canada. The PMRA requires similar chemistry and toxicology data for such import MRLs as those required to support Canadian food use registrations. In addition, the PMRA requires residue data that are representative of use conditions in exporting countries, in the same manner that representative

residue data are required to support domestic use of the pesticide. These requirements are necessary so that the PMRA may determine whether the requested MRLs are needed and to ensure they would not result in unacceptable health risks.

Presently, the *Pest Control Products Act* specifies MRL for tefluthrin residues in milk at a level of 0.001 ppm. Residues in all other agricultural commodities, including those approved for treatment in Canada but without a specified MRL, are covered in the Food and Drug Regulations, subsection B.15.002(1). This requires that residues do not exceed 0.1 ppm and has been considered a general MRL for enforcement purposes. Currently, residues of tefluthrin in corn are regulated by subsection B.15.002(1). However, changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*.

Residue data were available to indicate, that the existing MRLs should not be exceeded if tefluthrin is used according to good agricultural practice, as described by the current product labels. The submitted residue data for corn were adequate to show that residues in all corn commodities would not exceed 0.06 ppm, which is the combined limit of quantification for the residue analytical methods used to determine the parent tefluthrin and metabolite Ia in corn. Based on this data, an MRL at a level of 0.06 ppm will be proposed.

8.1.1.3 Proposed Mitigation for Mixer, Loader and Applicator Exposure and Postapplication Exposure

Use Precautions

Bystander exposure to insecticides is of potential concern. However, since tefluthrin is a relatively heavy, solid, granular formulation that is applied directly to the ground and incorporated into the dirt, no drift is expected. No bystander exposure is expected from members of the public walking, working or playing on treated soil, as tefluthrin is not registered for use in residential settings and no drift from any agricultural settings is anticipated.

Accidental exposure to tefluthrin is a possibility which necessitates the following label statement for all products:

"Keep the following personal protective equipment immediately available for use in case of emergency (in other words, a broken package, spill or equipment breakdown): chemical-resistant coveralls, chemical-resistant gloves, chemical-resistant head gear and a respirator."

Engineering Controls and Personal Protective Equipment

Statements must be amended (or added) to include the following directions to the appropriate labels in order to mitigate the risk of exposure to tefluthrin:

A. Mixing and loading granules:

Open mixing and loading with maximum PPE: Chemical resistant coveralls over a single layer (long sleeved shirt, long pants, socks plus shoes) with chemical resistant gloves, plus a suitable respirator.

Note that a closed mixing and loading system is not recommended, as the registrant has indicated that this is not a feasible mitigation measure.

B. Applying granules by tractor drawn broadcast spreader:
Use a closed cab with maximum PPE: Chemical resistant coveralls over a single layer (long sleeved shirt, long pants, socks plus shoes). Chemical resistant gloves for all tasks outside of the closed cab.

Restricted-entry Intervals
As a precautionary measure, the restricted-entry interval of 12 hours for all postapplication activities must be added to the product label.

8.1.2 Proposed Regulatory Action Related to Environment

To reduce the release of tefluthrin into the environment for the protection of terrestrial and aquatic habitats that may contain sensitive species, the PMRA is proposing further risk-reduction measures which include:

• Additional advisory statements to reduce runoff and to protect non-target species.

Environmental mitigation statements are listed in Appendix VIII.

8.1.3 Proposed Regulatory Action Related to Value

There are no regulatory actions proposed at this time for the continued registration of tefluthrin.

8.2 Additional Data Requirements

8.2.1 Data Requirements Related to Chemistry

The following data are required to support the continued registration of tefluthrin:

DACO 2.13.4: Impurities of Human Health or Environmental Concern

Analytical data from five recent batches of the TGAI for the analysis of HCB, PCB, and the three isomers of TCB. Note that if HCB, QCB, and/or any of the three isomers of TCB are detected in the product at any level, a new SPSF will be required which includes:

A) the nominal concentration (NC), lower and upper certified limits (LCL and UCL) for the active ingredient;
B) the NC and UCL for all impurities present in the product above 0.1%; and
C) the NC and UCL for all impurities of Human Health or Environmental Concern (HCB, QCB, and TCBs) present in the product at any level.

8.2.2 Data Requirements Related to Toxicology

The following confirmatory data are required to support continued registration of tefluthrin:

DACO 4.5.12: Acute neurotoxicity study (due to the MoA of tefluthrin)
DACO 4.5.13: 90-day neurotoxicity study (due to the MoA of tefluthrin)

DACO 4.5.14: Developmental neurotoxicity study (due to the central nervous system effects noted throughout the database and the quantitative sensitivity of the offspring in the two-generation reproduction study in rats)

8.2.3 Data Requirements Related to Occupational Exposure Assessment

No data are requested at this time.

8.2.4 Data Requirements Related to Food Residue Chemistry

The following confirmatory data are required to support continued registration of tefluthrin:

DACO 6.2: Poultry metabolism study to confirm goat metabolism data
DACO 7.2.2: Validated enforcement methods for all components of the tefluthrin residue definition in animal tissue, milk and eggs

The following data may be required for continued registration depending on the confirmatory data presented in the DACO 6.2 data gap:

DACO 7.5: Poultry and egg residue data from feeding of treated crops

8.2.5 Data Requirements Related to the Environment

No data are requested at this time.

8.2.6 Data Requirements Related to Value

No data are requested at this time.

List of Abbreviations

a.i.	active ingredient
ADI	acceptable daily intake
ARfD	acute reference dose
bw	body weight
°C	degree(s) Celsius
CAS	Chemical Abstracts Service
cm	centimetre(s)
d	day(s)
DT_{50}	dissipation time to 50% (the time required to observe a 50% decline in concentration)
DT_{90}	dissipation time to 90% (the time required to observe a 90% decline in concentration)
EC_{50}	effective concentration on 50% of the population
EDE	estimated daily exposure
EEC	estimated environmental concentration
FIR	food ingestion rate
g	gram(s)
GC	gas chromatography
GLC	gas liquid chromatography
GLC-ECD	gas liquid chromatography-electron capture detector
GLC-MS	gas liquid chromatography-mass spectrometry
h	hour(s)
ha	hectare(s)
HCB	hexachlorobenzene
hrs	hours
K_d	adsorption coefficient
K_f	Freundlich adsorption isotherm
kg	kilogram(s)
K_{oc}	organic carbon partition coefficient
K_{ow}	octanol–water partition coefficient
L	litre(s)
LC_{50}	lethal concentration on 50% of the population
LD_{50}	lethal dose on 50% of the population
LOC	Level of Concern
m	meter
mg	milligram(s)
min(s)	minute(s)
mL	millilitre(s)
mm	millimetre(s)
µg	microgram(s)
MoA	mode of action
MOE	margin of exposure
nm	nanometre(s)
NOAEL	no observable adverse effect level

NOEC	no observed effect concentration
NOEL	no observed adverse effect level
OM	organic matter
PCB	pentachlorobenzene
pH	-log10 hydrogen ion concentration
PHED	Pesticide Handlers Exposure Database
PPE	personal protective equipment
PMRA	Pest Management Regulatory Agency
RQ	risk quotient
SFS	Subjective facial sensation
TCB	tetrachlorobenzene
TGAI	technical grade active ingredient
TP	transformation product
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency
wk	week
Y	yes
yr	year

Appendix I Registered Tefluthrin Products as of 12 May 2008

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee
22616	Technical	Syngenta Crop Protection Canada Inc.	Tefluthrin Technical Insecticide	Solid	94%
23917	Commercial	Syngenta Crop Protection Canada Inc.	Force 3.0G Insecticide	Granular	3%

Appendix II Registered Commercial Class Uses of Tefluthrin in Canada as of 12 May 2008

Sites	Pests	Formulation Type[1]	Application Methods and Equipment	Application Rate (g a.i.)[3]		Maximum Number of Applications per Year	Typical Number of Days Between Applications	Supported Use?[2]
				Maximum Single	Maximum Cumulative			
USC 13 Terrestrial feed crops USC 14 Terrestrial food crops								
Corn, field Corn, sweet Corn, seed	Black cutworm Northern corn rootworm Western corn rootworm	GR	Banded: Apply insecticide in a 15–20 cm wide band centered over the seed furrow. The band should be applied ahead of the planter's press wheels and then incorporated into the top 1–2 cm of the soil.	Banded: 1.125 g/100 m row (≈ 112.5–150 g/ha)	Banded: 1.125 g/100 m row (≈ 112.5–150 g/ha)	1	Not applicable	Y
Corn, field Corn, sweet Corn, seed	Black cutworm Northern corn rootworm Seed corn maggot Western corn rootworm Wireworms	GR	In-Furrow: Apply insecticide in the furrow with the seed 2–5 cm deep. Insecticide should be applied directly behind the seed tube into the open seed furrow.	In-Furrow: 1.125 g/100 m row (≈ 112.5–150 g/ha)	In-Furrow: 1.125 g/100 m row (≈ 112.5–150 g/ha)	1	Not applicable	Y

1 GR = Granular

2 Y = use is supported by the registrant.

3 Rate range per hectare (ha) assumes a row spacing of 0.75 to 1.0 m.

Appendix III Toxicology Assessment for Tefluthrin

Table 1 Toxicity Profile of Technical Tefluthrin

NOTE: Effects noted below are known or assumed to occur in both sexes unless otherwise specified.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Metabolism/Toxicokinetic Studies			
Metabolism/ Toxicokinetic Study—rats (4/sex/time-point)	▪ Single oral doses of 1 or 10 mg/kg bw [^{14}C] labelled tefluthrin by gavage ▪ *Biliary fistula study*: single oral dose of 1 mg/kg bw [^{14}C] labelled tefluthrin by gavage ▪ Vehicle: corn oil ▪ Unlabelled: 99.1% Purity; [^{14}C] acid labelled tefluthrin: 97% Purity; [^{14}C] alcohol labelled tefluthrin: ≥96% Purity		**Absorption:** Based on the high amount of radiolabel present in the feces at 24 hrs, absorption may be incomplete. **Distribution:** The percent recovered in the liver, kidney, abdominal fat, blood and carcass was similar for both the acid labelled and the alcohol labelled tefluthrin. *After 2 hrs*: at 1 mg/kg bw (♂ and ♀) and 10 mg/kg bw (♀) the highest concentrations of radiolabel were identified in whole blood and plasma. *After 6 hrs*: at 1 mg/kg bw (♂ and ♀) and 10 mg/kg bw (♀) the peak concentrations of radiolabel were noted in the liver followed by the kidneys. At 10 mg/kg bw (♂) the highest concentrations of radiolabel were noted in the whole blood and plasma. *After 24 hrs*: at 10 mg/kg bw (♂) the peak concentration of radiolabel was noted in the liver. *After 48 hrs*: at 1 mg/kg bw the majority of the radiolabel was detected in the liver. A small amount of radiolabel was evident in the kidney. Little or no radioactivity was seen in bone, spleen, heart, gonads, lungs, brain, whole blood or plasma, consequently the residual activity after 7 days was not examined in these organs. *After 168 hrs*: a small amount of radiolabel was identified in the liver (less than 1.5% of the dose) at 1 mg/kg bw (♂ and ♀) and 10 mg/kg bw (♂) or fat at 10 mg/kg bw (♀). **Metabolism:** Tefluthrin was completely metabolized since there was no unchanged parent compound in bile or urine. Rates and routes of elimination of the radioactivity in the urine were similar for acid and alcohol labelled tefluthrin but the metabolic profiles were different. The metabolic products that were formed were extensively conjugated with the exception of 2,3,5,6-tetrafluoro-4-hydroxymethylbenzoic acid and 2,3,5,6-tetrafluoro-4-methylbenzoic acid which are excreted as free metabolites.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			Metabolites isolated from urine: *Major metabolites:* Metabolite 2: 2,3,5,6-tetrafluoro-4-methylbenzyl alcohol glucuronide Metabolite 4: Cis-3-(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropanecarboxylic acid *Minor metabolites:* Metabolite 1: 2,3,5,6-tetrafluoro-p-xylene-α,α′-diol Metabolite 3: 4-carboxy-2,3,5,6-tetrafluorobenzyl cis-3-(Z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropane-carboxylate Metabolite 5: Cis-3-(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethyl-cyclopropane-carboxylic acid ***Metabolites isolated from feces***: *Minor metabolites:* Metabolite 6: 2,3,5,6-tetrafluoro-4-hydroxymethylbenzyl cis-3-(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropane-carboxylate Metabolite 7: 2,3,5,6-tetrafluoro-4-methylbenzyl cis-3-(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclo-propane-carboxylate Metabolite 8: 2,3,5,6-tetrafluoro-4-hydroxymethylbenzyl cis-3-(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropane-carboxylate Metabolite 9: 2,3,5,6-tetrafluoro-4-hydroxymethyl benzoic acid **Excretion:** The excretion pattern was similar for both the acid and alcohol labelled tefluthrin. The majority of radioactivity was excreted within 72 hrs with most radiolabel recovered in urine and feces by day 7 (larger proportion excreted through the fecal route). Radioactivity expired as carbon dioxide accounted for less than 0.5% of the dose. **1 mg/kg bw:** *After 24 hrs:* excreted 16–33% of the dose in the urine and 25–52% of the dose in the feces. *After 168 hrs:* excreted 20–33% of the dose in the urine and 54–67% of the dose in the feces. **10 mg/kg bw:** *After 24 hrs*: urinary excretion was 16–17% of the dose and fecal excretion was 18–23% of the dose. *After 168 hrs*: urinary excretion was 26–33% of the dose and fecal excretion was 63–68% of the dose.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
		***Biliary fistula study*:** **Biliary Excretion** *After 48 hrs*: 41–46% of the dose was excreted via the feces, 3–7% via the urine and 5–16% in the bile (♂); 10–36% was excreted via the feces, 2–5% via the urine and 8–10% in the bile (♀).	
Metabolism/ Toxicokinetic Study—rats (3 treated ♀ & 1 control ♀ per time-point)	• 1 mg/kg bw (in corn oil) daily by oral gavage for a maximum of 14 days • Unlabelled: 99.1% Purity; [^{14}C] alcohol labelled tefluthrin: 97% Purity	**Distribution:** The radioactivity in all tissues consistently increased during the dosing period suggesting a potential for bioaccumulation. The highest levels of radioactivity were seen in the liver on day 14 of dosing with levels falling rapidly reaching a low by day 29 after dosing ($t_{1/2}$ = 4.8 days). The highest remaining radioactivity measurements on day 14 were found in the fat, ovaries, kidney and blood. The half-lives for tefluthrin in these organs ranged from 9.5 days (kidney) to 13.5 days (ovaries) on days 22–43. Levels in other tissues measured at 14 days were very low and included lungs, spleen, heart, bone, muscle and brain. **Metabolism:** Tefluthrin was found to be the major component in the fecal extract, along with other more polar metabolites. There was an increase in the proportion of polar metabolites in the urine after repeat dosing as compared to the animals from the single dose study. **Excretion:** The pattern of elimination was similar to that after a single oral dose of 1 mg/kg bw. *After 24 hrs*: urinary excretion was 39% of the dose and fecal excretion was 51% of the dose. *After 48 hrs*: urinary excretion was 44% of the dose and fecal excretion was 65% of the dose. *After 168 hrs*: urinary excretion was 49% of the dose and fecal excretion was 75% of the dose*. *Total radiolabel recovered by 7 days was 124%, since this figure only took into account the last 1 mg/kg bw of administered tefluthrin.	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Absorption and Metabolism in Fat—rats (12 ♀)	▪ 3 mg/kg bw (mixture of acid & alcohol labelled tefluthrin) daily by oral gavage for 14 consecutive days, 24 hrs after last dose abdominal fat was excised ▪ Vehicle: corn oil ▪ Unlabelled: 99.1% Purity; [^{14}C] acid labelled: 97% Purity, [^{14}C] alcohol labelled: >99% Purity	**Absorption:** Radioactivity in the fat had a half-life of 13 days and declined by a first order process. **Metabolism:** Analysis of the residue in fat revealed approximately half of the radioactivity was unchanged tefluthrin. The other half was found to contain two components that were likely fatty acid esters of hydroxylated tefluthrin metabolites. The predominant fatty acid appeared to be palmitic acid; oleic acid esters were also detected. 2,3,5,6-tetra-fluoro-4-methylbenzyl cis-3(z-2-chloro-3,3,3-trifluoroprop-1-enyl)-2-hydroxymethyl-2-methylcyclopropanecarboxylate was the most abundant of the hydroxylated tefluthrin metabolites, based on hydrolysis experiments.	
Metabolism/ Toxicokinetic Study—dogs (3/sex)	▪ Single oral dose of 1 mg/kg (by capsule) ▪ Vehicle: corn oil ▪ Unlabelled: 99.1% Purity; [^{14}C] alcohol labelled tefluthrin: 96.9% Purity	**Absorption:** The absorbed oral dose of tefluthrin peaked by 4–6 hrs (♂/♀) in the blood and declined rapidly thereafter. The presence of tefluthrin in the feces showed that absorption was incomplete. **Distribution:** Radioactivity dropped significantly by 96 hrs after dosing. The liver retained most of the labelled tefluthrin, followed by body fat (♀ had slightly higher radioactivity than ♂), kidneys and blood. **Metabolism:** No unchanged tefluthrin was excreted in the bile or urine. **Excretion:** The excretion profiles were similar between the sexes: *After 24 hrs*: urinary excretion was 18–19% of the dose and fecal excretion was 46–52% of the dose. *After 96 hrs*: urinary excretion was 25–27% of the dose and 66–70% of the dose was found in the feces.	
Acute Toxicity Studies			
Acute Oral Toxicity—mice (5/sex/dose)	▪ 9.8, 23.4 (♂ only), 48.0, 97.0 or 125 mg/kg bw (in corn oil) ▪ 90.4% Purity	**LD_{50} = 45.6/56.5 mg/kg bw (♂/♀)** **Highly Acutely Toxic**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Acute Oral Toxicity—rats (5/sex/dose)	▪ 10.1, 25.5, 47.0 or 100 mg/kg bw (in corn oil) ▪ 90.4% Purity	**LD_{50} = 21.8/34.6 mg/kg bw (♂/♀)** **Highly Acutely Toxic**	
Acute Inhalation Toxicity—rats (5/sex/dose)	▪ 7.7, 14.9, 39.9 or 60.5 mg/m^3 (= 0.008, 0.015, 0.040, or 0.061 mg/L) (in ethanol), nose only exposure ▪ 96.0% Purity	**LC_{50} = 0.049/0.037 mg/L (♂/♀)** **Highly Acutely Toxic**	
Acute Dermal Toxicity—rats (5/sex/dose)	▪ 50 (♀ only), 100, 500, 1,000 or 2,000 mg/kg bw, undiluted, under occlusive dressing for 24 hrs (up to 1,000 mg/kg bw) or for 2 hrs for all animals at 2,000 mg/kg bw and 1♀ at 1,000 mg/kg bw due to discomfort ▪ 90.4% Purity	**LD_{50} = 316/177 mg/kg bw (♂/♀)** **Highly Acutely Toxic**	
Dermal Irritation—rabbits (6♂/group)	▪ Undiluted test substance (0.5 mL) applied under an occlusive dressing for 4 hrs ▪ Draize test ▪ 90.4% Purity	**Slight to Minimal Dermal Irritant**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Eye Irritation— rabbits (6♂)	▪ Test material (0.1 mL) instilled into conjunctival sac after pretreatment with i.v. analgesic ▪ 5/6 animals received a 2nd dose of analgesic and 1/5 received a 3rd dose ▪ 90.4% Purity		**Severe Eye Irritant**
Eye Irritation— rabbits (2♂)	▪ Irrigated eye: 0.1 mL of test substance (1♂), 20-30 seconds later eye was rinsed for 1 min, scored at: 5–6 hrs ▪ Non-irrigated eye: dose lowered to 0.01 mL, instilled into eye (1♂), scored at: 1–2 & 3–4 hrs ▪ 90.4% Purity	Both rabbits showed initial pain reaction following the instillation of test substance. *Irrigated eye*: slight to moderate redness, slight to mild chemosis and extreme discharge observed up to 5–6 hrs after instillation and irrigation of the eye. After 6 hrs, the rabbit was killed due to severe pain and discomfort. *Non-irrigated eye*: slight conjunctival redness and moderate discharge observed at both reading times. 0.75 hrs after instillation of test substance the rabbit showed some discomfort. 3 hrs later the pain became severe and the rabbit was killed. **This study is considered supplemental.**	
Dermal Sensitization— guinea-pigs ▪ Maximization Test (Control group: 10♀; Test group: 20♀)	▪ *Intradermal Induction*: 2.5% and 5% tefluthrin (in corn oil) ▪ *Topical Induction*: 5.0% tefluthrin (in corn oil) ▪ *Challenge*: 10% and 50% tefluthrin (in corn oil) ▪ 90.4% Purity		**Not a potential Skin Sensitizer**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Subchronic Toxicity Studies			
28-Day Dietary Range-Finding Toxicity Study—Albino mice (15/sex/dose)	▪ 0, 25, 75, 200 or 400 ppm (= 0, 3.8, 11, 30 or 60 mg/kg bw/day) ▪ 90.4% Purity		*60 mg/kg bw/day*: ↓ bwg; ↓ bw (♀). **This study is considered supplemental.**
90-Day Dietary Toxicity Study—Wistar rats (20/sex/dose)	▪ 0, 50, 150 or 350 ppm (= 0, 2.5, 7.5 or 17.5 mg/kg/day) ▪ 90.4–93.0% Purity	7.5	**Males:** *≥7.5 mg/kg bw/day*: ↑ plasma cholesterol, ↑ relative liver wts (*not considered adverse*); 17.5 mg/kg bw/day: pallor of the retina, ↓ bw and bwg, ↓ FC, ↑ plasma urea levels, ↑ WBC, ↑ neutrophils, ↑ relative liver wts. **Females:** *7.5 mg/kg bw/day*: ↓ WBC, neutrophil and lymphocyte counts (*not considered adverse*); *17.5 mg/kg bw/day*: ↓ bw and bwg, ↓ FC, ↓ cholesterol and triglycerides, ↑ plasma urea levels.
13-day Oral Range-finding Toxicity Study—New Zealand White rabbits (0, 2, 6 and 15 mg/kg bw/day: 8♀/dose; 30 and 60 mg/kg bw/day: 4♀/dose)	▪ 0, 2, 6, 15, 30 or 60 mg/kg bw/day (in corn oil) by gavage for 13 days, left untreated for 9 days ▪ 90.4% Purity		*15 mg/kg bw/day*: neurotoxic effect (tremors) seen on study days 10–15 (1♀); *≥30 mg/kg bw/day*: severe neurotoxic effects seen in all animals, sacrificed on day 1, 2 or 3 of dosing. *60 mg/kg bw/day*: pale kidneys, rectum distended with gas, distended caecum, small intestine with white striations and containing yellow/green semi-solid material. **This study is considered supplemental.**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
6-Week Oral Range-Finding Toxicity Study—Beagle dogs (1/sex/dose)	▪ 0, 0.25, 1.0, 3.0 (1♂), 5.0 or 15.0 mg/kg bw/day (in corn oil) by capsule ▪ 95.1% Purity		*On study day 7, all animals were inadvertently double-dosed. More severe effects were seen shortly after misdosing with recovery by the following dosing. *1.0 mg/kg bw/day*: occasional vomiting noted throughout study, gait abnormalities noted in both animals after double-dosing; minimal signs of neurotoxicity including three occasions unrelated to mis-dosing (1♂); minimal signs of neurotoxicity on one occasion on the day of mis-dosing (1♀); *3.0 mg/kg bw/day (♂)*: severe signs of neurotoxicity (whole body tremors, ataxia, uncoordinated gait, pupillary dilatation, excessive salivation) 2–6 hrs after dosing and occasionally lasting for 24 hrs, ↓ bwg, sacrificed at 6 wks due to neurotoxicity; *5.0 mg/kg bw/day*: severe signs of neurotoxicity (whole body tremors, ataxia, uncoordinated gait, pupillary dilation, excessive salivation) 2–6 hrs after dosing and occasionally lasting for 24 hrs (♂ more sensitive than ♀), ↓ bwg, ♂ sacrificed on day 4 due to neurotoxicity, ♀ sacrificed on day 25 due to neurotoxicity;

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			15.0 mg/kg bw/day: ♂ sacrificed on day 3 due to neurotoxicity, ♀ found dead on day 8 (24 hrs after being double-dosed) with the following alterations noted: ↓ FC, ↓ glucose, ↑ cholesterol (wk 1), mucosal congestion and epithelial necrosis at base of mucosal glands in jejunum, colon and rectum, lympholysis of submucosal lymphoid tissue. **This study is considered supplemental.**
90-day Oral Toxicity Study— Beagle dogs (4/sex/dose)	▪ 0, 0.1, 0.5 or 1.5 mg/kg bw/day (in corn oil) by capsule ▪ 95.1% Purity	♂: 1.5 mg/kg bw/day ♀: 0.5 mg/kg bw/day	**Males:** *1.5 mg/kg bw/day*: ↑ triglyceride levels (4, 8 and 13 wks) (*not considered adverse*). **Females:** *1.5 mg/kg bw/day*: body tremors on day 4 three hrs after dosing (full recovery within an hour) (1♀), transient ↑ in CK and ↓ ALP, ↑ absolute and relative thyroid wts.
1-year Oral Toxicity Study— Beagle dogs (6/sex/dose)	▪ 0, 0.1, 0.5 or 2.0 mg/kg bw/day (in corn oil) by capsule ▪ 95.1% Purity	0.5	**Males:** *>0.1 mg/kg bw/day*: slightly ↓ bwg, ↑ frequency of fluid feces (*not considered adverse*); *>0.5 mg/kg bw/day*: slightly ↓ Hgb, Hct and RBC counts (*not considered adverse*); *2.0 mg/kg bw/day*: neurotoxicity (ataxia, unsteady gait and body tremors) primarily during the first month of treatment (3/6), vomiting (1/6), ↓ bwg, ↑ plasma triglyceride levels, ↑ relative liver and kidney wts, one animal with whole body tremors, bleeding from

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			hind claws and an unsteady gait, this animal also vomited paint flakes and 1 nematode on day 57, found dead on day 252. **Females:** *2.0 mg/kg bw/day*: neurotoxicity (ataxia (6/6), unsteady gait (5/6), body tremors (3/6) and vomiting (3/6)) primarily during the first month, ↑ frequency of fluid feces, 1 animal displayed bilateral optical neuritis, choroiditis and scleritis with focal unilateral retinal degeneration with mononuclear cell infiltration.
21-day Dermal Toxicity Study—Wistar rats (10/sex/dose)	• 0, 1, 5 or 50 mg/kg bw/day (in polyethylene glycol) to test sites (clipped and intact) under a semi-occlusive dressing for 6 hrs/day • Purity 90.4%	1	**Males:** *1 mg/kg bw/day*: ↓ WBC and lymphocyte counts (*not considered adverse*); *5 mg/kg bw/day*: abnormal gait (2♂), ↓ plasma triglyceride, protein and albumin levels, ↓ WBC and lymphocyte counts, ↓ relative kidney wts; *50 mg/kg bw/day*: 1 mortality on day 6 (unknown cause), flicking of front paws and exaggerated lifting of hind limbs (4♂), tremors/shaking (3♂), abnormal gait (10♂), ↓ bw and bwg, ↓ plasma triglyceride, cholesterol, albumin and total protein levels, ↓ WBC and lymphocyte counts, ↑ K^+ levels, ↓ absolute and relative liver wts, acanthosis, necrosis of the epidermis and inflammatory cell infiltrate of the dermis.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			Females: *1 mg/kg bw/day*: ↓ plasma Mg^{+2} levels (not considered adverse); *5 mg/kg bw/day*: 1 animal sacrificed on day 15 due to malocclusion, abnormal gait (7♀), flicking of front paws and exaggerated lifting of hind limbs (3♀), ↓ plasma triglycerides and Mg^{+2} levels; *50 mg/kg bw/day*: flicking of front paws and exaggerated lifting of hind limbs (7♀), tremors/shaking (3♀), abnormal gait (10♀), ↓ bwg, ↓ plasma total protein and phosphorus levels, ↓ plasma Mg^{+2} levels, acanthosis, necrosis of the epidermis and inflammatory cell infiltrate of the dermis.
Chronic Toxicity/Oncogenicity Studies			
2-year Dietary Carcinogenicity Study—AP mice (50/sex/dose)	• 0 (2 groups), 25, 100 or 400 ppm (= 0, 3.4, 13 or 54 mg/kg bw/day) • Purity 95.1%	3.4	**Males:** *3.4 mg/kg bw/day*: ↓ WBC (*not considered adverse*); *13.5 mg/kg bw/day*: abnormal gait (1/50), ↓ hindlimb function (2/50), ↓ bwg, ↓ WBC & ↑ lymphocyte counts, ↑ absolute and relative liver wts, congestion in the spleen;

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			54.4 mg/kg bw/day: clonic convulsions (1/50), abnormal gait (2/50), reduced hindlimb function (1/50), tip toe gait (1/50), ↓ bwg, ↓ mean final bw, ↓ FC, ↓ FE, ↑ WBC and lymphocyte counts, ↑ absolute and relative liver wts, ↓ absolute and relative testicular wts, congestion in the spleen. **Females:** *3.4 mg/kg bw/day*: ↓ WBC & lymphocyte counts (*not considered adverse*); *13.5 mg/kg bw/day*: ↑ activity (1/50), ↓ WBC and lymphocyte counts, hepatocyte necrosis, endometrial hyperplasia of the uterus, hemangiomatous change of the uterus, ectopic cutaneous adnexa of the ovary; *54.4 mg/kg bw/day*: ↓ survival rate towards end of study, abnormal gait (1/50), clonic convulsions (2/50), splayed gait (1/50), ↓ bwg, ↓ mean final bw, ↓ FC, ↓ FE, ↓ WBC and lymphocyte counts, ↑ relative liver wt, hemorrhage in the spleen, hepatocyte pigmentation, hepatocyte necrosis, hepatic telangiectasis (dilation of the capillary vessels), ectasia of the mammary gland, endometrial hyperplasia of the uterus, hemangiomatous change of the uterus, ovarian necrosis, ectopic cutaneous adnexa of the ovary, atrophy of hair follicles, parakeratosis.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			Neoplastic findings: *Hepatic Type A Nodules (hyperplastic nodules as well as benign tumours)*: ↑ incidence in high-dose ♀(1/50, 1/50, 0/49, 3/50 and 5/50* at 0, 0, 3.4, 13.5 and 54.4 mg/kg bw/day, resp.). *Historical control data for Hepatic Type A Nodules*: ♀: mean of 2.2% (range of 0.0 to 3.8%). Evidence of tumourigenicity in females.
2-year Dietary Toxicity Study—Wistar rats (Main study: 52/sex/dose; Interim kill at 1 year: an additional 12/sex/dose; Satellite study for control and high-dose groups: an additional 12/sex)	▪ 0, 25, 100 or 400 ppm (= 0, 1.1, 4.6 or 18.2 mg/kg bw/day) ▪ In the first 3 wks a number high-dose animals died ▪ Interim sacrifice at 52 wks ▪ 95.1% Purity	1.1	***Terminal Sacrifice*:** **Males:** *4.6 mg/kg bw/day*: abnormal and splayed gait (4♂), ↑ response to sound (3♂), ↓ bwg, ↓ FC and FE, ↑ ALP, ↑ incidence of minimal foci of hepatocellular alteration and hepatic spongiosis; *18.2 mg/kg bw/day*: ↑ mortality (4♂, first 3 wks, unknown cause), ↑ activity and tremors (1♂), abnormal and splayed gait (7♂), ↑ response to sound (1♂), ↓ bwg, ↓ FC and FE, ↑ AST and ALT activities, ↑ ALP, ↓ urine volume, ↑ incidence of sinusoidal hemorrhage of the mesenteric lymph node, minimal foci of hepatocellular alteration and hepatic spongiosis. **Females:** *4.6 mg/kg bw/day*: abnormal and splayed gait (7♀), ↓ bw and bwg, ↑ AST, ↓ urine volumes; *18.2 mg/kg bw/day*: ↑ mortality (5♀ during first 3 wks, unknown cause), ↑ response to sound (14♀), ↑ activity and tremors (2♀), abnormal and splayed gait

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			(60♀), ↓ bw and bwg, ↓ FC and FE, ↑ plasma AST and ALT activities, ↓ ALP, ↓ urine volume, ↑ relative liver wts, ↑ relative brain wts, ↑ incidence of uterine luminal distension, cervical fibromuscular hyperplasia, unilateral cataracts, pituitary cysts and cystic ovaries. *Interim Kill*: Males: *18.2 mg/kg bw/day*: ↑ relative liver and brain wts. Females: *≥4.6 mg/kg bw/day*: ↑ absolute and relative ovarian wts; *18.2 mg/kg bw/day*: ↑ relative liver and brain wts, ↑ absolute and relative ovarian wts. *Neoplastic findings*: *Adenocarcinoma of the Uterus:* ↑ incidence in high-dose ♀ (2/61, 0/52, 2/52 and 5/56 at 0, 1.1, 4.6 and 18.2 mg/kg bw/day, resp.). *Historical control data for Adenocarcinoma of the Uterus:* ♀: mean of 2.4% (range of 0.0 to 5.8%). Evidence of carcinogenicity in females.
Developmental/Reproductive Toxicity Studies			
Dietary Reproductive Toxicity Study—Wistar rats (2-generation) (15♂ F_0 and 30♀ F_0 parents/dose)	• 0, 15, 50 or 250 ppm (= 0, 0.7, 2.5 or 12 mg/kg bw/day) • 95.1% Purity	Parental = 2.5 Reproductive = 2.5 Offspring = 0.75	**Parental:** *Control group had the highest intercurrent deaths among all groups. ***F_0 generation:*** *12 mg/kg bw/day*: high-stepping gait (1♂; 4♀), ↓ bw and FC; abnormal/splayed gait (7♀), ↓ bw (during gestation), bwg (during gestation) and FE (♀).

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			***F_1 generation*:** *12 mg/kg bw/day*: ↓ bw, bwg and FC; animals sacrificed due to poor clinical condition (2♀), animal found dead at wk 17 (1♀, unknown cause), ↓ bw (during gestation) and bwg (during gestation), ↑ FE, abnormal/splayed gait (2♀) (♀). **Reproductive:** *F_0 generation*: *12 mg/kg bw/day*: ↓ mean litter size at birth and mean total litter wt at birth. ***F_1 generation*:** *12 mg/kg bw/day*: ↓ mean litter size at birth (F_{2B}), ↓ pup survival due to a high incidence of litter losses (F_{2A}), shorter median pre-coital intervals (F_{2B}). **Offspring:** *F_1 generation*: *12 mg/kg bw/day*: ↓ bwg, ↓ litter weight gain (F_{1A} and F_{1B}), ↑ incidence of shaking (day 22: 1 F_{1B} pup) and abnormal/splayed gait (day 30: 12 F_{1A} pups from 1 litter). ***F_2 generation*:** *2.5 mg/kg bw/day*: ↑ incidence of shaking (day 5: 7 F_{2B} pups from 1 litter, day 22: 2 F_{2A} pups from 2 litters); *12 mg/kg bw/day*: ↓ bwg, ↓ litter weight gain (F_{2A} and F_{2B}), ↓ number of litters and number of pups on day 29 (F_{2A}), ↓ mean litter size on day 29 (F_{2A} and F_{2B}),↑ incidence of shaking (day 22: 57 F_{2A} pups from 9 litters and 174 F_{2B} pups from 19 litters; day 29: 58 F_{2A} pups from 7 litters and

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			209 F_{2B} pups from 20 litters) and abnormal/splayed gait (day 22: 8 F_{2A} pups from 4 litters; day 29: 3 F_{2A} pups from 2 litters).
Oral Developmental Toxicity Study— Wistar rats (24 mated ♀: 0, 1, 3 and 5 mg/kg bw/day; 18 mated ♀: 7.5 mg/kg bw/day; 6 extra mated ♀: 0 mg/kg bw/day)	▪ 0, 1, 3 or 7.5 mg/kg bw/day (in corn oil) by gavage on GD 6-15 (the day of confirmation of mating was defined as GD 0), dams killed on GD 21 ▪ Due to an unacceptably high level of mortalities in the 7.5 mg/kg bw/day group, an additional dose level (5 mg/kg bw/day) and a concurrent vehicle control group were added ▪ 93% Purity	Parental = 1 Develop-mental = 3	**Maternal:** *3 mg/kg bw/day* : ↑ incidence of subdued behaviour (2/24), ↓ bwg and FC (GD 7–10); *5 mg/kg bw/day*: ↑ incidence of abnormal gait (7/24), hypersensitivity (19/24), piloerection (19/24) and subdued behaviour (24/24), ↓ bwg and FC (GD 7–10), ↑ number of early intra-uterine deaths; *7.5 mg/kg bw/day*: ↑ mortalities (7/18), ↑ incidence of abnormal gait (15/18), uncoordinated limb movements (12/18), involuntary movement/spasms/convulsions of the limbs (8/18), partial loss of the use of the hind limbs (6/18), coat staining (6/18), damaged tails (6/18), signs of incontinence (4/18), hypersensitivity (9/18), piloerection (6/18) and subdued behaviour (11/18), gastro-intestinal tract changes at necropsy (7). **Offspring:** *5 mg/kg bw/day*: ↑ fetal incidence of 25th pre-sacral vertebrae (5/184 pups from 3/24 litters) (historical control data: 0–0.3% of fetuses and 0–4.2% of litters). **No evidence of teratogenicity**
Oral Range—Finding Developmental Toxicity Study - NZW rabbits	▪ 0, 5, 10 or 20 mg/kg bw/day (in corn oil) by gavage on GD		**Maternal:** *10 mg/kg bw/day*: ↑ incidence of subdued

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
(8 mated ♀/dose)	6–18 (day of insemination was considered to be GD0) ▪ 90.4% Purity		behaviour and tremors (1♀); *20 mg/kg bw/day*: ↑mortality (3♀ found dead), 2 animals sacrificed, ↑ incidence of subdued behaviour (4♀) and tremors (6♀, 4 of which were also subdued). No effects were seen on litter or fetal parameters. **This study is considered supplemental**.
Oral Developmental Toxicity Study—NZW Rabbits (18 mated ♀/dose)	▪ 0, 3, 6 or 12 mg/kg bw/day (in corn oil) by gavage on GD 6–18 (the day of insemination was designated as GD 0), dams sacrificed on GD 29 ▪ 93.0% Purity	Maternal LOAEL = 3 Develop-mental LOAEL = 3	**Maternal:** *>3 mg/kg bw/day*: 1♀ found dead on GD15 (1.5 hrs after dosing, exhibited dilated pupils and moderate to extreme body tremors just prior to death); *6 mg/kg bw/day*: 1♀ found dead on GD17 (laboured breathing, mucus around eyes and nose and diarrhea all observed on GD17), ↑ incidence of body tremors (1♀), ↓ bwg (GD7–10 and GD16–19) and FC (GD7–19); *12 mg/kg bw/day*: 1♀ sacrificed in moribund condition on GD13 (tremors on GD9–12, subdued and unable to use legs on GD13), ↑ incidence of tremors (6♀), ↓ bwg (GD7–10 and GD16–19) and FC (GD7–19). **Developmental:** *>3 mg/kg bw/day*: ↑ incidence of fetuses with extra 13th ribs and 27th pre-sacral vertebrae. **No evidence of teratogenicity**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Genotoxicity Studies			
In vitro Studies			
In vitro, Reverse mutation assay • *Salmonella typhimurium*	▪ 0, 0.02, 0.08, 0.4, 2, 10 or 50 mg/mL (in DMSO)± activation, 2 trials ▪ 95.1% Purity		**Negative**
In vitro, Mouse Lymphoma TK +/- Forward Mutation Assay • L5178Y cells	▪ 0, 250, 500, 1,000, 2,000 or 4,000 μg/ml (in DMSO) ± activation, 5 experiments, 3 w/ expression time of 72 hrs & 2 w/expression time of 48 hrs ▪ 90.4% Purity		**Negative**
In vitro, Unscheduled DNA synthesis ▪ Primary Hepatocytes from ♂ AP rats	▪ $1.0x10^{-9}$ to $1.0x10^{-2}$ M (in DMSO) ▪ 2 experiments ▪ 95.1% Purity		**Negative**
In vivo Studies			
In vivo, Dominant Lethal Study CD-1 mice (15 ♂/group; 2♀/each ♂ mated each week for 8 consecutive weeks)	▪ 0, 1, 3 or 10 mg/kg bw (in corn oil) by gavage daily for 5 consecutive days ▪ 90.4% Purity		**Negative**
In vivo, Micronucleus AssayC57/BL/6J mice (5/sex/dose/ time point)	▪ 0, 31 or 50 mg/kg bw (in corn oil) by single i.p. injection, animals killed at 24, 48 and 72 hr time points ▪ 95.1% Purity		**Negative**

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
In vivo, Cytogenicity Assay ▪ Bone marrow from AP rats (*Main experiment*: *Control*: 12/sex/ time point; *2.5, 12.5 & 25 mg/kg bw*: 8/sex/time point; *Repeat experiment*: 24 hrs: *0 mg/kg bw*: 12 ♀, *25 mg/kg bw*: 8♀; 48 hr sacrifice: *0 mg/kg*: 11♀, *2.5, 12.5 & 25 mg/kg bw*: 8♀)	▪ Main and repeat experiments: 0, 2.5, 12 or 25 mg/kg bw (in corn oil) by gavage ▪ Sacrificed according to the following schedule: *main experiment*: *0 & 25 mg/kg bw*: 12, 24 & 48 hrs; *2.5 & 12.5 mg/kg bw*: 24 hrs; *repeat experiment*: *0 & 25 mg/kg bw*: 24 & 48 hrs; *2.5 & 12.5 mg/kg bw*: 48 hrs ▪ 90.4% Purity	**Main Experiment** ***Chromosome Analysis*:** *48 hr bone marrow samples*: ↑ incidence of abnormalities evident in ♀ treated w/25.0 mg/kg bw which was statistically significant when chromosome gaps (2/7) were included, a higher percentage of chromosome minutes (3/7) were evident, a higher proportion of females was also affected (85.7% vs 58.3% in controls) (only 7♀ were included at this time point, no explanation provided). ***Mitotic Indices*:** *12 hr bone marrow samples*: ↓ in ♂ and ♀ at 25.0 mg/kg bw; *48 hr bone marrow samples*: ↓ in ♀ at 25 mg/kg bw. Due to evidence of a possible clastogenic effect in females noted at 25 mg/kg bw at the 48 hr sampling time, a repeat experiment was conducted using only female rats. **Repeat Experiment (in ♀ only):** ***Chromosome Analysis and Mitotic Indices*:** Results were comparable between negative controls and tefluthrin-treated females. The results of first study were not reproduced in the repeat experiment; therefore, tefluthrin is considered non-clastogenic. **Negative**	
Other Toxicity Studies			
Oral Acute Delayed Neurotoxicity Study—Domestic Hens (10♀/group; one control group, one positive control group and 4 tefluthrin-exposed groups)	▪ Single dose of 0 or 3,800 mg/kg bw (in corn oil) by gavage on day 1 followed by a repeat dose of 0 or 3,780 mg/kg bw (in corn oil) by gavage on day 21 to birds that demonstrated a negative neurotoxic response ▪ Positive control: TOCP – 500 mg/kg bw by gavage ▪ 94.4% Purity	*0 mg/kg bw:* 2 mortalities after first dose, 0 mortalities after second dose; *3,800 mg/kg bw:* 20 mortalities out of 40 hens after first dose; *3,780 mg/kg bw:* 7 mortalities out of the remaining 20 hens after second dose (leaving 13 survivors); *500 mg/kg bw TOCP*: 4 mortalities after first dose (only one dose given). Effects observed in hens dosed w/tefluthrin included: subdued behaviour, unsteadiness, stumbling, trembling, wing flapping, inability to stand, lying on one side, unable to walk and eyes closed with head and neck rotating. First signs were noted within 1 hr of dosing and were most frequent and severe on days 1 and 2. The majority of birds that survived had recovered on days 5 and 6. Similar signs of toxicity were observed after the second tefluthrin dose. The majority of survivors recovered by day 26.	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
			No signs of delayed neurotoxicity were observed in tefluthrin treated hens. Body weight gain was reduced between days 1 and 21 and was increased from day 22 to 42. Food consumption was reduced from day 1 to 42. There were no treatment-related gross macroscopic findings. All tefluthrin treated hens that survived (13 hens) displayed grade II changes (disruption or fragmentation of occasional axons, myelin abnormalities were rare) in at least 2 levels of the spinal cord (similar to negative controls) and 5/13 hens also showed grade III changes (disruption, fragmentation or distortion of a few axons, changes in myelin sheaths were minimal and usually consisted of small spheroids) in at least 1 level of spinal cord. One hen showed grade II changes in 1 level of peripheral nerve and 2 hens showed grade II changes in the brain. The grade III changes observed were indicative of axonal degeneration and were possibly related to treatment. Signs of acute delayed neurotoxicity were not definite since no significant axonal degeneration was observed in peripheral nerve and the distribution of lesions in the spinal cord was not typical in some hens (ie. not confirmed to the upper cervical region). No signs of delayed neurotoxicity.
Neurotoxicity Study—Alderley Park Albino rats (10 rats/sex/ group)	▪ Animals were administered either vehicle, 2,5–hexanedione (positive control) or tefluthrin (5 or 15 mg/kg bw) by gavage, 5 days per wk for 8 wks ▪ Behavioural & neuro-physiological assessments (including tail nerve conduction velocities) performed at weekly intervals ▪ Purity N/S		*5 mg/kg bw/day*: all ♀s and 1♂ animal were found dead on day 2, the ♀s that died were replaced on day 2, for the first 3 weeks animals failed to gain weight at the same rate as control animals; from week 3 onward tefluthrin treated animals gained weight at the same rate as controls, 2♀s were found dead in their cages (on days 5 and 51) with no clinical signs of toxicity previously observed in either animal to account for the deaths; *15 mg/kg bw/day*: all animals were found dead on day 2. *Pull-up test for detection of muscle weakness*: Transient increase in the time taken to complete the test in ♀s (week 1) and ♂s (week 2) were recorded. *Nerve conduction velocity measurements*: Mean motor nerve conduction velocity (MNCV) and motor nerve action potentials (MNAP) in tefluthrin treated animals were unaffected. Sensory nerve conduction velocity (SNCV) was reduced in ♂s (weeks 2 and 4). Amplitude of the sensory nerve action potentials (SNAP) was also reduced in week 2 in both ♂s and ♀s and in week 3 in ♂s and week 6 in ♀s. Tefluthrin treated rats that survived the dosing showed no evidence of peripheral neuropathy.

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
Acute Range-finding Neurotoxicity Study—Sprague Dawley rats (5 ♂/group)	▪ 0, 5, 10 or 15 mg/kg bw (in corn oil) by gavage ▪ Neuro-behavioural assessment (FOB test) performed at 2, 4 and 8 hrs post-dosing ▪ Additional dosage levels (0, 15 or 20 mg/kg bw) evaluated at 4, 6 and 8 hrs in order to characterize the neurotoxic effects & the time of peak effect ▪ 92.4% Purity	There were no test article-related deaths or moribundities at ≤15 mg/kg bw tefluthrin while 2♂ at 20 mg/kg bw were euthanized prior to the observation at 6 hrs. The predominant findings in the FOB evaluation included tremors, gait abnormalities and whole body convulsions. Peak effects were noted at 8 hours post-dosing. **This study is considered supplemental.**	
Acute Neurotoxicity Study—Sprague Dawley rats (10 ♂/group)	▪ 0, 10 or 15 mg/kg bw (in corn oil) by gavage ▪ Neuro-behavioural assessment (FOB test) performed at 8 hrs post-dosing ▪ 92.4% Purity	The FOB findings noted in this study were limited to effects on the central nervous system (CNS) and included: clonic convulsions (twitches, irregular jerking movements of the limbs, whole body), slight tremors and bizarre/stereotypic behaviour (head flick). Tefluthrin exposed males also exhibited gait abnormalities such as impaired mobility, splayed hindlimbs, hunched body, ataxia and exaggerated hindlimb flexion. Tefluthrin exposed animals also exhibited a slight effect on coordination of the air righting reflex and a dose-related decrease in grip strength for both the forelimbs and hindlimbs. Note: no neuropathological examination was conducted. **This study is considered supplemental.**	
Acute Oral Toxicity—Wistar rats (5/sex/dose) Metabolite of Tefluthrin: R173,204	▪ 5,000 mg/kg bw (in corn oil) by gavage ▪ Observations made up to 15 days post-dosing ▪ 98% Purity	*5,000 mg/kg bw*: 0/10 mortalities. All animals (both genders) showed signs of toxicity on day 1 persisting in two animals up to and including day 3. The most common signs of toxicity were signs of diarrhea, dehydration, salivation and urinary incontinence. **This study is considered supplemental.**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
In vitro, Effects on Chloride Ion Channels ▪ Mouse neuroblastoma cells (N1E-115)	▪ Tefluthrin dissolved in DMSO at a concentration of 10 µM with 5 replicates, grown in DMEM culture medium ▪ Positive control: Deltamethrin ▪ 98.8% Purity	Open channel probability was calculated as the proportion of time that current, attributed to chloride ion flux across a single ion channel was observed during the recording period. Tefluthrin had no affect on the chloride ion channels from the mouse neuroblastoma cells. **This study is considered supplemental.**	
In vitro, Action of Pyrethroids on Calcium Influx and Glutamate Release from Isolated Presynaptic Nerve Terminals from Rat Brain ▪ Sprague Dawley rats (♀) synaptosomes	▪ Concentrations of tefluthrin ranged from $2x10^{-17}$ to $2x10^{-5}$ M ▪ 8 replicates per synaptosome preparation ▪ 95.0% Purity	Tefluthrin failed to elicit a concentration-dependent response, suggesting that voltage-sensitive calcium channels were not involved in the action of this compound. As well, tefluthrin demonstrated a relatively low potency in the glutamate release assay. **This study is considered supplemental.**	
Toxicological Effects in Humans			
A survey of farm operators and ICI personnel in the United Kingdom (conducted in 1987) ▪ Certain synthetic pyrethroids cause SFS— transient tingling, burning or numb feeling of the skin, usually of the face	▪ Survey conducted to determine occurrence of SFS as a result of exposure to tefluthrin ▪ formulations: 20% capsule suspension or granular formulation of tefluthrin containing 5.0 g tefluthrin/kg ▪ Worker exposure trials conducted at a total of 17 sites ▪ Purity N/S	At 3 of 17 trial sites, symptoms of SFS were observed: A. One operator noticed a burning sensation at a very localised spot on the face after 1 hr of using the granular formulation. The symptoms disappeared overnight. The exposure occurred when the operator removed his face mask to check if hoppers containing the formulation were emptying. B. A second operator noticed a tingling sensation of the face, forehead and cheekbones ~4 hrs after starting to use tefluthrin (formulation type not specified). Gloves, faceshield and overalls were worn while filling the hoppers of the drill and when calibrating. Faceshield and gloves were removed during the drilling operation. Symptoms of SFS disappeared overnight. C. A third operator experienced a cold sensation in the eye when a granule entered the right eye when uncoupling the vacuum cleaner to empty the granules out of the dust bag. Symptoms occurred 5 mins later and subsided after 6 hrs. **Considered supplemental.**	

Study/Species/ # of animals per group	Dose Levels/Purity of Test Material	NOAEL (mg/kg bw/day)	Results/Effects
A user acceptability study was performed at the ICI Japan Agricultural Research Station, Tsukuba City (conducted in 1988)	▪ 25 operators each exposed to 1 kg of a granular formulation (0.5% tefluthrin) and a similar formulation (no active ingredient) to assess any SFS arising from application ▪ Application performed on 'double blind' basis (1 hand for tefluthrin, other hand for blank), on completion of each application operators lightly stroked the same sides of their faces 3 times with the middle 3 fingers of the corresponding hand ▪ Purity N/S	All 25 operators were asked to return a questionnaire, but 1 failed to return it. SFS was recorded in 11 subjects. Of these, 5 were classified as true positive responses, 4 as false positive and 2 as true/false (symptoms could not be positively identified as SFS but may have been). Symptoms of SFS included tingling, burning and itching mainly on the face. The intensity of the sensations were described as mild to moderate and disappeared within 20 mins to 8 hrs. The operator who felt SFS at 8 hrs had symptoms which were extremely mild and had to consider whether he felt any sensations or not. The quickest response time was 5 mins and the longest response time was 90 mins, with the average being 20 mins. Effects of SFS in operators were not severe or distressing enough to require treatment. **Considered supplemental.**	

Table 2 Toxicology Endpoints for Use in Health Risk Assessment for Tefluthrin

Exposure Scenario	Endpoint	Study	Dose (mg/kg bw/day)	CAF or MOE[a]
Acute Dietary	Maternal toxicity (subdued behaviour, decreased food consumption and body weight gain)	An oral (gavage) teratogenicity study in the rat	1	1000
	ARfD = 0.001 mg/kg bw			
Chronic Dietary	Signs of neurotoxicity along with decreased body weight gain	An oral (by capsule) 12-month study in the dog	0.5	1000
	ADI = 0.0005 mg/kg bw/day			
Short- and Intermediate-term Dermal	Signs of neurotoxicity	A 21-day dermal toxicity study in the rat	1	1000
Short- and Intermediate-term Inhalation	Signs of neurotoxicity along with decreased body weight gain	An oral (by capsule) 12-month study in the dog	0.5	1000
Cancer Risk Assessment	An adjusted Q_1^* value of 3.07×10^{-2} $(mg/kg\ bw/day)^{-1}$ from the two-year chronic toxicity/carcinogenicity study in rats based on the increased incidence of adenocarcinoma of the uterus in females.			

Exposure Scenario	Endpoint	Study	Dose (mg/kg bw/day)	CAF or MOE[a]
Aggregate Risk Assessment— Food and Drinking Water	The most relevant studies are those selected for the Acute Reference Dose and the Acceptable Daily Intake for acute and repeated exposure scenarios, respectively.			

[a] CAF (composite assessment factor) refers to total of uncertainty and *Pest Control Products Act* factors for dietary assessments, MOE refers to desired margin of exposure for occupational or residential assessments.

[b] Since an oral NOAEL was selected, an inhalation absorption factor of 100% (default value) should be used in route-to-route extrapolation.

Appendix IV Agricultural Mixer/Loader/Applicator and Postapplication Risk Assessment

Table 1 Mixer/Loader/Applicator Exposure Estimates and MOEs

Crop	Form [a]	Application Equipment	Application Rates [b] (kg a.i./ha)	Area treated per day [c] (ha)	Daily Exposure (µg/kg/day)		Margins of Exposure		Combined MOEs [h]
					Dermal [d]	Inhalation [e]	Dermal [f]	Inhalation [g]	
Mixing and Loading: Open mix/load with maximum PPE. Applying: Closed cab with maximum PPE.									
corn (field, sweet and seed)	GR	broadcast spreader	0.15	80	0.81	0.47	1233	1072	574
Mixing and Loading: Open mix/load with maximum PPE and a suitable respirator. Applying: Closed cab with maximum PPE.									
corn (field, sweet and seed)	GR	broadcast spreader	0.15	80	0.19	0.13	1233	3941	939

Maximum PPE = Chemical resistant coveralls over a single layer (long sleeved shirt with long pants), socks plus shoes and chemical resistant gloves.

[a] GR = Granular

[b] Maximum listed label rate in kilograms of active ingredient per hectare (kg a.i./ha).

[c] Based on registrant response data and default assumptions, see Section 3.7 for details.

[d] Where dermal exposure µg/kg/day = (unit exposure × area treated × rate)/70 kg bw.

[e] Where inhalation exposure µg/kg/day = (unit exposure × area treated × rate)/70 kg bw. A 90% protection factor was incorporated into the inhalation data for respirators.

[f] Based on a dermal NOAEL of 1.0 mg/kg bw/day and a target dermal MOE of 1000.

[g] Based on an oral NOAEL of 0.5 mg/kg bw/day and a target inhalation MOE of 1000.

[h] Combined MOE = 1 / ((1/Dermal MOE)+(1/Inhalation MOE)). Shaded cells indicate calculated combined MOEs that fail to meet the target of 1000.

Table 2 Mixer/Loader/Applicator Cancer Risk Assessment

Crop	Form [a]	Application Equipment [b]	Active ingredient handled per day (kg)	Total Absorbed Daily Dose [b] (ADD) (mg/kg /day)	Treatment Days Per Year	Total Lifetime Absorbed Daily Dose [c] (LADD) (mg/kg bw)	Cancer Risk [d]
Mixing and Loading: Open mix/load with maximum PPE. Applying: Closed cab with maximum PPE.							
corn (field, sweet and seed)	GR	broadcast spreader	12	0.0013	30	5.25E-05	2.0E-06
Mixing and Loading: Open mix/load with maximum PPE and a suitable respirator. Applying: Closed cab with maximum PPE.							
corn (field, sweet and seed)	GR	broadcast spreader	12	0.0009	30	3.85E-05	1.0E-06

Maximum PPE = Chemical resistant coveralls over a single layer (long sleeved shirt with long pants), socks plus shoes and chemical resistant gloves.

[a] GR=Granular.
[b] Absorbed Daily Dose = daily dermal dose + daily inhalation dose, as determined by PHED scenarios.
[c] LADD=ADD × treatment frequency × working duration/ (365 days × 75 years). Lifetime = 75 years, Treatment frequency = 30 days/year, Working duration = 35 years.
[d] A Q_1^* value of 3.07E-02 $(mg/kg/day)^{-1}$ was considered appropriate to use in the cancer risk assessment.

Appendix V Dietary Exposure and Risk Estimates for Tefluthrin

Table 1 Acute Dietary Exposure and Risk for Tefluthrin

Population Groups	Food		Food and Water	
	Exposure[1] (mg/kg bw/day)	% ARfD[2]	Exposure[1] (mg/kg bw/day)	% ARfD[2]
General Population	0.000305	30.6	0.000307	30.7
All Infants (<1 year old)	0.000727	72.7	0.000758	75.8
Children 1–2 years old	0.000559	55.9	0.000561	56.1
Children 3–5 years old	0.000518	51.8	0.00052	52
Children 6–12 years old	0.000393	39.3	0.000394	39.4
Males 13–19 years old	0.000351	35.1	0.000353	35.3
Males 20–49 years old	0.00023	23	0.000233	23.3
Adults 50+ years old	0.000152	15.2	0.000155	15.5
Females 13–49 years old	0.00023	23	0.000234	23.4

1 99.9th percentile of exposure

2 ARfD for all population groups was based on a NOAEL of 1 mg/kg bw/day from an oral (gavage) teratogenicity study in the Wistar rat based on maternal toxicity in the form of decreased food consumption, body weight gain and subdued behaviour at the next dosage level of 3 mg/kg bw/day; composite assessment factor of 1000 was applied.

Table 2 Chronic Non-Cancer Dietary Exposure and Risk for Tefluthrin

Population Groups	Food		Food and Water	
	Exposure (mg/kg bw/day)	% ADI[1]	Exposure (mg/kg bw/day)	% ADI[1]
General Population	0.000011	2.2	0.000012	2.4
All Infants (<1 year old)	0.000016	3.2	0.000019	3.8
Children 1–2 years old	0.000046	9.1	0.000047	9.4
Children 3–5 years old	0.000034	6.7	0.000035	7
Children 6–12 years old	0.000021	4.2	0.000022	4.4
Youth 13–19 years old	0.000011	2.1	0.000011	2.3
Adults 20–49 years old	0.000007	1.4	0.000008	1.6
Adults 50+ years old	0.000006	1.2	0.000007	1.4
Females 13–49 years old	0.000007	1.4	0.000008	1.6

[1] ADI for all populations based on NOAEL of 0.5 mg/kg bw/day from a 12-month oral (by capsule) study in beagle dogs established based on signs of neurotoxicity, including ataxia, unsteady gait, body tremors and vomiting along with decreased body weight gain in both males and females at the next dosage level of 2 mg/kg bw/day; composite assessment factor of 1000 was used.

Table 3 Chronic Cancer Dietary Exposure and Risk for Tefluthrin

Population Group	Lifetime Cancer Risk[1]	
	Food	Food and Water
General Population	0.3×10^{-6}	0.4×10^{-6}

[1] Cancer Unit Risk (Q_1^*) based on bioassay data from a two-year chronic toxicity/carcinogenicity study in rats, Q_1^* value of 3.07×10^{-2} (mg/kg bw/day)$^{-1}$ was used.

Appendix VI Food Residue Chemistry Summary

1.1 Metabolism

The nature of the residues in ruminants and plants is understood. However, there are inadequate data to characterize the metabolism in poultry. A poultry metabolism study is recommended to supplement the livestock metabolism database.

1.1.1 Plant metabolism

Two metabolism studies were performed on corn with tefluthrin radiolabelled in the cyclopropane and in the phenyl ring. In the studies, a sandy loam soil was treated with a granular formulation of tefluthrin containing ^{14}C-cyclopropane or ^{14}C-phenyl radiolabelled material at a rate of 3.76 mg a.i./507 cm^2 on a 17.5 cm band. This rate is equivalent to 1.30 g a.i./100 m row with a band of 17.5 cm width. The treated soil was potted, planted with corn seeds and kept under greenhouse condition until maturity (69–76 days after germination). The analysis of the total radioactive residue composition containing ^{14}C-cyclopropane radiolabelled material is presented in Table 1:

Table 1 Metabolite composition in ^{14}C-cyclopropane labelled tefluthrin treated corn leaves

Metabolites		% of total residues
Tefluthrin		5
Metabolite	Ia	11.5
	XI	13.3
Water solubles		18
Unextractable		13.7
Unknown		12.6
At origin (TLC)		30.9
Losses		2

The analysis of the total radioactive residue composition containing ^{14}C-phenyl radiolabelled material is listed in Table 2:

Table 2 Metabolite Compositions in ^{14}C-phenyl Labelled Tefluthrin Treated Corn Leaves and Stem

Metabolites		% of total residues	
		Leaves	Stem
Tefluthrin		<1.0	N.D.
Metabolite	IV	3.8	N.D.
	VI	58.3	64.2
Water solubles		3.7	5.7
Unextractable		6	19
Unknown		5.8	6.7
At origin (TLC)		4	-
Losses		13.4	5.5

The metabolites of concern are the parent compound – tefluthrin (PP993) and the metabolite Ia (PP890) which can be found in a ratio of 5:11.5 in corn commodities. Based on the submitted data, tefluthrin is metabolised quickly to a variety of compounds derived from the cyclopropane or phenyl ring.

1.1.2 Animal metabolism

A goat metabolism study performed on a single subject was submitted for the analysis of the metabolism of the tefluthrin treated animals. In this study a lactating goat was dosed orally twice daily with ^{14}C-tefluthrin (radiolabelled in the cyclopropane ring and in the tetrafluoro-4-methylbenzyl ring, for 4 days at a rate equivalent to 10.9 mg a.i./kg total diet. The goat was euthanized 16 hrs after the last dose intake and several samples were taken for analysis.

Tefluthrin is rapidly, but partially, absorbed by the oral routes, completely metabolized and subsequently excreted via the urine. Examination of the radioactivity excreted in the urine (41.4% of the dose) showed that extensive metabolism occurs in the goat, so that no unchanged tefluthrin was present in the urine. Some unchanged tefluthrin was detected in the faeces (28.7% of the administered dose), but most (74 %) of the total radioactivity recovered in the tissue was present as metabolites of tefluthrin.

Extensive metabolism occurred in the goat by ester cleavage and oxidation at a variety of positions on the molecule. Low radioactive residues were detected in the milk (0.076 ppm), fat (0.076 ppm) and muscle (0.016 ppm), with tefluthrin as the largest individual component of the residue (milk 66.5%, fat 76.7%, muscle 34.2%). Higher residues were present in the kidney (0.3 ppm) and liver (1.0 ppm) and only a small percentage of this residue was due to tefluthrin (kidney 3.4%, liver 6.1%). The remainder of the residue in the kidney and liver was a complex mixture of metabolites. Most of the kidney metabolites were identified, but a high proportion of the liver residue was due to six unidentified polar compounds.

The total residue level in goat samples is listed in Table 3 and the metabolites are characterized in Table 4.

Table 3 Residue Levels in Tissue Samples Originated from Treated Goat

Sample	Sampling Time	Radioactive Residue Concentration (ppm)
Diaphragm muscle	End of 4th day	0.063
Fore-quarter muscle		0.016
Hind-quarter muscle		0.013
Subcutaneous fat		0.059
Omental fat		0.076
Perirenal fat		0.068
Kidney		0.307
Liver		0.834–1.000
Milk	Day 1	0.000–0.005
	Day 2	0.028–0.053
	Day 3	0.052–0.076
	Day 4	0.056–0.072
	Day 5	0.062

Table 4 Characterization of Radioactive Residues in Tissue Samples

Compounds	% Total Radioactive Residue in Tissue Samples				
	fat	diaphragm muscle	muscle	kidney	liver
Tefluthrin	76.5	54.0	34.2	3.4	6.2
Compound VII	-	-	2.0	15.2	6.0
II	-	3.3	-	-	-
XI	1.0	-	-	8.9	10.2
Ia	1.7	6.3	18.6	26.0	5.5
VIII	2.8	3.8	-	0.2	1.9
IX	11.4	-	-	5.0	4.5
VI	-	-	-	9.1	2.8
III	0.8	-	-	8.6	-
Solubles	2.8	-	-	-	2.6
Solide	2.7	15.3	12.1	-	11.7
Polar compounds	-	11.0	16.2	11.8	35.4
Unknown A	-	-	2.7	6.7	5.8
B	-	-	4.7	-	-
C	-	-	-	-	1.4
Activity lost	-	-	4.0	-	-
Remainder	-	6.3	5.5	5.6	5.9
ppm equivalent	0.076	0.067	0.014	0.312	0.870

Since low tefluthrin residues were detected in treated corn grains, straw, and forage samples, tefluthrin exposure to ruminants from crop feeds is expected to be minimal.

1.1.3 Canadian and International MRLs

When pesticides are used on crops or when animals are fed crops treated with pesticides, residues may remain in or on the food when it is sold. PMRA must determine the amount of residues that are likely to remain in or on the food when the pesticide is used according to label directions and poses no unacceptable risks to human health. This amount is then legally established as the MRL under the *Pest Control Products Act*. Pesticides that do not have established MRLs on food commodities are covered by the general MRL under subsection B.15.002 (1) of the Food and Drugs Regulation of the *Food and Drugs Act* (≤0.1ppm). A summary of tefluthrin Canadian and international MRLs are provided in Table 5. There are no MRLs for tefluthrin listed in the Codex Alimentarius.

Based on field trial data, an MRL of 0.06 ppm on corn is proposed.

Table 5 Tefluthrin Canadian and International Maximum Residue Limits

Canadian MRL (ppm)	
Milk	0.001
US Tolerance (ppm)[1]	
Corn, field fodder and forage, pop and sweet	0.06
Corn, fresh (including sweet corn and corn with husk, removed (CWHR)	0.06
Corn, field, grain and pop	0.06

[1] Covered under Part B, Division 15, subsection B.15.002(1) of the Food and Drug Regulations as ≤0.1 ppm

1.1.4 Residue Definition

The residue definition is used to describe the sum of the parent pesticide, its degradation products, metabolites and impurities that are of toxicological concern. All components of the residue definition will normally be included in the MRL expression of the pesticide, and residue analytical methods must be developed for all components of the residue definition.

Based on metabolism data, the current residue definition in all commodities is the parent compound, tefluthrin (2,3,5,6-tetrafluoro-4-methylbenzyl (Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2- dimethylcyclopropanecarboxylate) including metabolites containing the (cis-3-(Z-2-chloro-3,3,3,trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate) moiety.

A new residue definition and MRL are proposed for the corn commodities as following: tefluthrin (2,3,5,6-tetrafluoro-4-methylbenzyl (Z)-(1RS)-cis-3-(2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2- dimethylcyclopropanecarboxylate) (PP993), and its metabolite Ia: (Z-3-(2-chloro-3,3,3,trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid) (PP890).

1.2 Analytical Methods

1.2.1 Methods for Residue Analysis in Plant

Several gas liquid chromatography (GLC) methods were developed to analyze tefluthrin in different commodities. These methods are listed in Table 6.

The submitted analytical methods are gas chromatography (GC) or GLC methods that are based on extraction methods of the samples performed mainly with a water:acetonitrile mixture followed by an solid-phase extraction/silica clean-up. The samples are then derivatized by methylation, silylation or benzylation and analysed by GC/GLC with electron capture detection or mass spectrometry detection. The analysed metabolites are parent tefluthrin (PP993), metabolite Ia (PP890) and metabolite VI (R173204) and the results show good recovery levels ranging from 52–127% and mean values from 74–102% for LOD's from 0.005 to 0.05 ppm.

Table 6 Summary of residue analytical methods in plants

Method code	Compound	Method	LOD (ppm)	Sample	PMRA Ref.
GRAM 029	compound VI	GC-MS	0.05	crops	1534051
RAM 85/1	tefluthrin	GLC-ECD	0.005–0.01	crops/soil	1534053
RAM 105	compound Ia	GLC-ECD	0.01	crops	1534054
	compound VI	GLC-ECD	0.01	crops	1534054
RAM130	compound VI	GLC-ECD	0.05	crops	1534055
GAM002/88	tefluthrin	GLC-ECD	0.01	crops/soil	1534056
GRAM028	compound Ia	GC-ECD	0.05	crops	1534058

1.2.2 Methods for Residue Analysis of Food of Animal Origin

Tefluthrin and metabolite concentrations in milk and animal products listed in Table 7 are analysed according to the methods RAM 104 and RAM 106. The method is applied to analysis of tefluthrin in milk, meat, kidney, liver or fat and has a limit of determination (LOD) of 0.001 ppm (milk) and 0.002 ppm (tissues) and metabolite Ia milk, meat, kidney, liver or fat with an LOD of 0.01 ppm. The samples fortified with an internal standard are extracted by homogenization with acetonitrile or acetone:hexane. Co-extracted lipids are removed by liquid-liquid partition chromatography followed by derivatization and Florisil adsorption chromatography. The quantitative determination is done by GLC-ECD and either internal or external standardisation. For tefluthrin (PP993) the repeatability of the measurements on muscle extracts is of +/- 1%, though by external standardisation this value is of +/- 14%. The correlation coefficient was r>0.99 and the recovering range was within 53.1–125% depending on the analysed tissue. For the metabolite Ia (PP890) the correlation coefficient was as well r>0.99 and the recovering range was within 56–105%.

Table 7 Summary of Residue Analytical Methods in Plants

Method code	Compound	Method	LOD (ppm)	Sample	PMRA Ref.
RAM104	Tefluthrin (PP993)	GLC-ECD	0.001	milk	1534057
			0.002	tissues	1534057
RAM 106	compound Ia /(PP890)	GC-ECD	0.01	milk, tissues	1683957
	compound VI	GC-ECD	0.01	milk, tissues	1683957

1.2.3 Independent Laboratory Validation

Independent laboratory validations were performed with good results for the residue analytical methods GRAM 029, GRAM 028 and RAM105 confirming the performance and validity of these residue analytical methods. The LOD of the methods were at 0.01 and 0.05 ppm with recoveries averaging 90–100%.

1.2.4 Multi-Residue Analytical Method

The method for the determination and quantitative analysis of tefluthrin is reported in the Pesticide Analytical Manual (PAM 1), established and revised by the United States Food and Drug Administration, and is listed in table 302a under the method 302(E1-E3+DG1-DG19)/(acetone extraction, partitioning or Hydromatrix removal of water, GLC determination with various columns or detectors), as stated under 40CFR180.6(d) and 180.101(c). As listed, the method was tested for recovery at 0.275 and 1.374 ppm.

The United States Food and Drug Administration proposed analytical method for the tefluthrin metabolites (PP890 and R173204—compound VI) was analysed in a validation study (RR 90-358B/1988; PMRA 1534060), where the analytical procedures were performed by an independent laboratory. The report concluded that the tefluthrin metabolites did not perform well on the GC and high performance liquid chromatography as it was described in PAM 1 and therefore the recovery studies for those compounds were not accomplished.

1.3 Food Residues

1.3.1 Storage Stability

1.3.1.1 Freezer Storage Stability in Plants

The storage stability of tefluthrin and metabolites in frozen crop samples at about -18°C, was analysed in various crop samples after fortification with a standard solution. The characteristics and results of the studies are listed in Table 8.

The storage stability studies reviewed indicate freezer storage stability for corn for up to 24 months and were found to be acceptable.

Table 8 Summary of storage stability studies in plants

Study	Metabolite	Commodity	Period (months)	T (°C)	Recovery (%)
1534067	PP993—parent	Corn	24	-18	104
1534069	PP890/R173204	Corn grain	24	-18	75/78
1534073	PP890/R173204	Corn	12–19	<0	—
1534074	PP993—parent	Corn	6	-20	104
534076	PP993/PP890	Corn	24/36	-20	102/88

1.3.1.2 Freezer Storage Stability in Animals

The storage stability study (PMRA 1534072) determined the storage stability of the tefluthrin residue in frozen bovine tissues and milk. The fortified samples (fortification level 0.002–0.01 ppm) were frozen at -20°C up to a period of seven months and analysed in terms of tefluthrin residue in milk, peritoneal and subcutaneous fat, adductor and pectoral muscle, kidney and liver. There were no significant changes in the residue levels in any tissue after the storage. The mean external recovery was 59% with a standard deviation of 9%.

Similarly, the study (PMRA 1219058) shows a good freezer storage stability at -18°C for milk (227 days), muscles (238 days), kidney (265 days), liver (247 days) and fat (399 days). For a fortification of 0.2 ppm the mean internal standard recovery for PP890 was 61% with a standard deviation of 20, and 71% ± 19 for R173204.

The summary of the mentioned stability studies is presented in Table 9.

Table 9 Summary of Storage Stability Studies in Animals

Study	Metabolite	Commodity	Period (months)	T (°C)	Recovery (%)
1534072	PP993—parent	Animal tissue, milk	7	-20	59
1219058	PP890/R173204	Animal tissue, milk	7–13	-20	61/71

1.3.1.3 Storage Stability of Working Solutions in Analytical Methodology

There are no storage stability studies for working/standard solutions. These are required for the complete assessment according to Regulatory Directive DIR98-02, *Residue Chemistry Guidelines;* therefore, it is recommended that the registrant submits this requested confirmatory data.

1.3.2 Crop Residues

CANADA

Eighteen residue trials (PMRA 1216906; 1216907; 1143317; 1534089) performed in Canada were analyzed for tefluthrin residues according to method RAM 85/1 on samples of immature/mature plants and grains taken 63–160 days after application, respectively. For fortifications of 0.1–0.2 ppm the recovery range was 91–103%, with an LOQ of 0.01 ppm. No measurable residue (<0.01 ppm) were identified in all crop samples.

UNITED STATES

By summarizing all field trials (PMRA 1534090; 1534088, 1534076; 1534091) performed on field corn crops in United States at label or higher application rates, the residues levels in various corn samples are presented in Table 10.

Table 10 Maximal Residue Values in Various Corn Samples (ppm)

	PP993	PP890	R173204
Forage	0.01	0.05	0.03
Silage	0.01	—	—
Ears	0.01	0.05	0.01
Cob	0.01	0.05	0.01
Kernel	0.01	0.05	0.01
Stover	0.01	0.01	—
Fodder	0.01	0.03	0.02
Stem	0.01	—	—
Leaves	0.01	—	—

The samples were collected 49–102 days after treatment for forage and 56–147 days after treatment for ears and grains. The samples were analysed for residues of tefluthrin parent (PP993) and metabolite Ia (PP890). The LOD of the analytical methods used were 0.005/0.01/0.05 ppm. At fortification levels ranging from 0.02–0.2 ppm the recoveries from different corn samples are listed in Table 11.

Table 11 Average Recoveries from Fortified Corn Samples

Residue		Tefluthrin		PP890	
Fortification (ppm)		0.02	0.4	0.05	0.4
Recovery	forage	119%	98%	78%	79%
	ears	111%	89%	85%	82%
	kernels	—	114%	99%	—
	cobs	101%	—	—	82%

Two studies (PMRA 1533919; 1533921) present the measurements of the total radioactive residues that were determined in leaves, stem and grains. The values obtained are presented in Table 12. The values indicate that the leaves present the highest radioactivity and contain the highest residue concentration.

Table 12 Total Radioactive Residues Found in Crop Samples

Crop sample	Label	Treatment rate g a.i./100m row	Radioactive residue concentration ppm		
			Treated	Control	Net value
Leaves	^{14}C Cyclopropane	1.30	0.091	0.033	0.058
Stem		1.30	0.017	0.005	0.012
Grain		1.30	0.017	0.009	0.008
Leaves	^{14}C Phenyl	1.43	0.492	0.033	0.459
Stem		1.43	0.086	0.005	0.081
Grain		1.43	0.013	0.009	0.004

It should be noted that the residue value obtained in corn leaves is high. Considering all the plant parts used in fodder production a mean value is calculated according to the weight proportion of leaves and stem in corn plants. According to the weight ratio of the leaves and stem (1:3), the average residue value for fodder would be 0.02 ppm and 0.18 ppm, respectively. However, according to the metabolic studies these total residue values contain only 16.5% of PP993 and 1% of PP890. The residue levels obtained in corn samples will be below 0.01 ppm PP993 and 0.005 ppm PP890.

All the residue results available indicated that a maximum of 0.06 ppm of total residues of the parent compound and its major metabolite could be found in corn samples when treated according to the label. Considering the residue decline, it is recommended not to harvest sweet or field corn for forage until 49 days after treatment and for cobs or grain until 56 days after treatment.

1.3.3 Livestock Residues

Two ruminant feeding residue reports (PMRA 1533918, 1219058) present the results of a study made on a group of 14 Friesian cows, which were fed for a period of 28 to 30 days, with a diet containing tefluthrin and its metabolite R173204. The three feeding rates studied were of 0.3, 0.9 and 3 mg tefluthrin/kg diet/day + 0.2, 0.6 and 2 mg R173204/kg diet/day, respectively. No residues were detected in animal samples of the two low feeding rates. The presented results from the highest feeding rate describe the tefluthrin, metabolite Ia and R173204 residue analysis. From the average milk yields and tefluthrin residue levels it can be calculated that between 0.2–0.4% of the daily dose was eliminated in the milk. When tefluthrin was removed from the diet, fourteen days after the end of the feeding, the residue level in milk decreased to under 0.001 ppm. At the residue level reached by tefluthrin in corn, low residue levels are expected to be found in milk, below the imposed MRL. Table 13 presents an overview of the residue values from the cow samples.

Table 13 Characterization of Tefluthrin Residues in Cow Samples

		Cow diet—3 mg tefluthrin/kg diet + 2 mg R173204/kg diet		
		Tefluthrin—PP993	**Metabolite Ia—PP890**	**R173204**
		Milk concentration ppm		
milk	after 5 days of diet	0.02	<0.01	0.01
	after 8 days of diet		<0.01	0.01
	after 10 days of diet	0.02		
	after 12 days of diet		<0.01	<0.01
	after 15 days of diet	0.02		
	after 17 days of diet		<0.01	<0.01
	after 24 days of diet		<0.01	0.01
	after 26 days of diet	<0.01		
	after 28 days (diet ceased)	<0.01	<0.01	<0.01
	after 30 days (diet ceased)	<0.01		
	after 34 days (withdrawal)	<0.001		
	after 37 days (withdrawal)	<0.001		
	after 40 days (withdrawal)	<0.001		
	after 43 days (withdrawal)	<0.001		
peritoneal fat		0.03–0.13	0.01–0.03	0.01–0.03
subcutaneous fat		0.03–0.13	<0.01	<0.01
kidney		0.003–0.004	0.01–0.02	<0.01–0.01
muscle		<0.002–0.005	<0.01	<0.01
liver		<0.002–0.002	0.01–0.02	<0.01–0.02

Residues of both metabolite Ia (PP890) and R173204 were below 0.01 ppm in muscle and subcutaneous fat samples from cows fed at the highest dietary level containing tefluthrin at 3 ppm and R173204 at 2 ppm. Residues (up to 0.03 ppm were found in the liver, kidney, and peritoneal fat samples but these decreased to below 0.01 ppm in the two cows from this group fed for fourteen days on untreated diet prior to slaughter. Therefore, metabolite residues transferred from the corn treated according to good agricultural practice, to the milk and animal tissues are expected to be below 0.01 ppm for tissue samples and below 0.001 ppm for milk.

1.3.4 Confined and Field Crop Rotation

Complete confined rotational crop studies (PMRA 1534080; 1534081) were performed with radiolabelled tefluthrin on straw and grains (wheat, millet), foliage (lettuce), foliage and beans (soy) and foliage and roots (sugar beet) at higher application rates than the labelled ones. Samples were taken and analysed from commodities replanted after 30/39, 121 and 401 days from the treatment. The total radioactive residue level in the crop samples reached levels up to 1.28 ppm. However, from the total radioactive residues, the residues of tefluthrin parent and metabolite Ia were below the LOD of the detection method—0.005 ppm for tefluthrin and 0.01 ppm for metabolite Ia.

Similarly, field rotational crop studies (PMRA 1534086, 1534082) were performed at labelled application rate on the same commodities. The replant interval for the analysed commodity was at 30 and 130/135 days after treatment in the first study and 26, 122 and 395 days after treatment for the second study. Samples of crops grown in the treated soil contained no measurable residues of tefluthrin or metabolite Ia at any replant interval. Table 14 presents the summary of the residues of tefluthrin and metabolite Ia at the 30 days replant interval. As all the representative crop commodities show residue levels below the level of concern, these values support the replant in the treated soil of rotational crops, 30 days after treatment.

Table 14 Residue Level in Crops Replanted After 30 Days

Crop	Residue level ppm		
	Tefluthrin	Metabolite Ia	Total residue
Lettuce	0.006	<0.01	<0.016
Turnip (Root/Leaf)	<0.005	<0.01	<0.015
Millet forage	<0.005	<0.01	<0.015
Millet grain/straw	<0.005	<0.01	<0.015
Soy forage	<0.005	<0.01	<0.015
Soy bean/hay	<0.005	<0.01	<0.015
Wheat Grain	<0.01	<0.05	<0.06

1.3.5 Processed Food/Feed Data

There are no processed food/feed studies submitted by the registrant. However, the registrant submitted a rationale (PMRA 1534049) stating that the residue of tefluthrin and his metabolites are not detectable in the corn kernels at an exaggerated rate of 10 times the registered rate. Therefore the registrant states that a processing study is not needed since no residue would be expected to be detected in any of the commercial processed fraction from corn kernels treated at a normal application rate. As the processing adjustment factor in different processed food does not exceed 1.5, the rationale is acceptable and no processed food studies are necessary.

Appendix VII Environmental Fate and Toxicity

Table 1 Toxic Substances Management Policy Considerations—Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Are criteria met?	Transformation Products Are criteria met?
Toxic or toxic-equivalent as defined by the *Canadian Environmental Protection Act**	Yes		Yes	No data
Predominantly anthropogenic**	Yes		Yes	Yes
Persistent***	Persistent in one of the following media:		Not persistent	No data
	Soil	Half-life ≥182 days	No. Half-life 63 d	No. Half-life 16 d
	Water	Half-life ≥182 days	No. Half-life 146 d	No data
	Sediment	Half-life ≥365 days	No. Half-life 204 d	No data
	Air	Half-life ≥2 days or evidence of long range transport	No. Half-life in air (0.94 d)	No data
Bioaccumulative****	Log K_{ow} ≥5		6 .4 Yes	No data
	BCF ≥5000		1400 No	No data
	BAF ≥5000		Not available	No data
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	No, does not meet TSMP Track 1 criteria.

* All pesticides will be considered toxic or toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the toxicity criterion may be refined if required (in other words, all other TSMP criteria are met).

** The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity rather than to natural sources or releases.

*** If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

**** Field data (for example, bioaccumulation factors) are preferred over laboratory data (such as bioconcentration factors), which, in turn, are preferred over chemical properties (for example, log K_{ow}).

Table 2 Fate and Behaviour in the Environment

Study type	Test material	Study Conditions	Value or Endpoint	Interpretation	Transformation products*	Reference
Abiotic transformation						
Hydrolysis	Tefluthrin	pH 5, 7 and 9. 25°C.	Stable at pH 5 and 7. pH 9 28% of parent transformed. Half life >30d.	Not an important route of transformation	Compound Ia 34.6% A.R. max. Compound II 21.4% AR. Max.	PMRA 1689035
Phototransformation—soil	Tefluthrin	Test duration 31 d with buried granular formulation. Volatilization of A.R. occurred.	DT_{50} not available. 58–79% A.R. in 14C cyclopropyl labeled and 79% A.R. in phenyl labelled tefluthrin	Not an important route of transformation	Compound unidentified 16–19% A.R. max.	PMRA 1689035
Phototransformation—water		25°C. Tes duration 31 d. Sterile water pH 7.	DT_{50} 11.2 d 60–63% of A.R. detected as tefluthrinafter 31 d.	Not an important route of transformation	Transtefluthrin 22–37% of A.R. max.	PMRA 1689035
Phototransformation—air	Tefluthrin	0.5×10^6 OH/cm^3	0.94 d	An important route of transformation if tefluthrin volatilizes to the atmosphere.		PMRA 1689035
Biotransformation						
Soil—aerobic	Tefluthrin	18 acres sandy loam. pH 6.8 20°C. Single First Order calculation.	DT_{50} 48 d DT_{90} 160 d	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	18 acres sandy loam. pH 6.8 20°C. Single First Order calculation.	DT_{50} 151 d DT_{90} NA granular application	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	Frensham sandy loam. pH 5.3 20°C. Single First Order calculation.	DT_{50} 63 d DT_{90} NA	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035

	Tefluthrin	18 acres sandy loam. pH 6.5 20°C. Single First Order calculation.	DT_{50} 13d DT_{90} 43d	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	18 acres sandy loam. pH 6.5 20°C. Single First Order calculation.	DT_{50} 20d DT_{90} 67d	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	18 acres sandy loam. pH 6.5 20°C. Single First Order calculation.	DT_{50} 26d DT_{90} 86d	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Transform. Product Ia.	18 acres sandy loam. pH 6.5 20°C. Single First Order calculation.	DT_{50} 16d DT_{90} 48d	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	18 acres sandy loam. pH 6.5 5°C. Single First Order calculation.	DT_{50} 34d DT_{50} 41d adjusted to 20°C	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	18 acres sandy loam. pH 6.5 30°C. Single First Order calculation.	DT_{50} 17d DT_{90} 58d DT_{50} 37d adjusted to 20°C	An important route of transformation.	Compound Ia 7.1% A.R. max. Compound III, IV and V <5% A.R.	PMRA 1689035
	Tefluthrin	Sandy clay loam 20°C.	DT_{50} 40d	An important route of transformation.	Compound III, IV and V	PMRA 1690207
	Tefluthrin	Sandy loam 20°C	DT_{50} 45d	An important route of transformation.	Compound III, IV and V	PMRA 1690207
	Tefluthrin	Clay loam 20°C	DT_{50} 22d	An important route of transformation.	Compound III, IV and V	PMRA 1690207
	Tefluthrin	Clay loam 20°C	DT_{50} 12d	An important route of transformation.	Compound III, IV and V	PMRA 1690207
	Tefluthrin	Sandy clay loam 20°C	DT_{50} 160d granular formulation	An important route of transformation.	Compound III, IV and V	PMRA 1690207
Soil— flooded Not anaerobic	Tefluthrin	Sandy loam. pH 6.8)M 4.6%. Flooded but not purged with N2. Airflow so not anaerobic	DT_{50} 150d	An important route of transformation.	Compound III 12% in soil, 6% AR in water.	PMRA (1993).

Water/ sediment— aerobic	Tefluthrin	Kromme Rijn, pH water 8.2, pH sediment 7.3, 20°C SFO calculation.	DT_{50} 146d whole system DT_{90} NA whole system DT_{50} 203 d sediment DT_{90} NA sediment	An important route of transformation.	Compound Ia 22% AR in water at day 84, max 7% AR in sediment, Compound II max 3% AR in water & sediment at day 7 Compound IV max 7% AR in water at day14 (22% at 5°C) Compound V 2.3% AR in water day 7 (6.6% in sediment and 7.9% in water at 5°C).	PMRA 1689035; 1657921
		TNO Zuidpolder, pH water 8.8, sediment 7.4, 20 °C, SFO calculation.	DT_{50} 60 d total system DT_{90} NA total system DT_{50} 204 d sediment only DT_{90} NA sediment only	An important route of transformation.	Compound Ia 22% A.R. max. in water day 84, 7% in sediment Compound II 3% iax in water & sediment day 7 Compound IV 7% AR max in water day 14 Compound V 2.3% max in water day 7.	PMRA1689035; 1657921.
		Old Basing ^{14}C-Cyclopropyl label. pH water 7.6, pH sediment 7.6, 20°C, SFO calculation.	DT_{50} 58 d total system DT_{90} 185 d total system DT_{50} 57 d sediment only DT_{90} 189 d sediment only	An important route of transformation.	Compounds Ia 22% AR in water at day 84, max 7% AR in sediment, Compound II max 3% AR in water & sediment at day 7, Compound IV max 7% AR in water at day14 (22% at 5°C) Compound V 2.3% AR in water day 7	PMRA 1689035; 1657918

		Old Basing ^{14}C-Phenyl label. pH water 7.6, pH sediment 7.6, 20°C. Single First Order calculation.	DT_{50} 51 d total system DT_{90} 185 d total system DT_{50} 59 d sediment only DT_{90} 195 d sediment only	An important route of transformation.	Compounds Ia 22% AR in water at day 84, max 7% AR in sediment, Compound II max 3% AR in water & sediment at day 7, Compound IV max 7% AR in water at day14 (22% at 5°C) Compound V 2.3% AR in water day 7	PMRA 1689035; 1657918
Water/ sediment—anaerobic	Tefluthrin	No data	No data			
Mobility						
Adsorption/ desorption	Tefluthrin	OC = 1.6%, pH 6.3, sandy clay loam.	K_d = 1800 K_{oc} = 112500 K_f = 1200 1/n = 0.93	Immobile.	Not reported	PMRA 1689035
		OC = 0.7%, pH 6.2, sandy loam.	K_d = 762 K_{oc} = 109000 K_f = 332 1/n = 0.83	Immobile.	Not reported	PMRA 1689035
		OC = 0.9%, pH 6.6, sandy loam.	K_d = 895 K_{oc} = 99500 K_f = 20521/n = 1.16	Immobile.	Not reported	PMRA 1689035
		OC = 0.4%, pH 5.2, silt loam.	K_d = 1067 K_{oc} = 267000 K_f = 14400 1/n = 1.5	Immobile.	Not reported	PMRA 1689035
		OC = 1.7%, pH 5.8, sandy loam.	K_d = 1140 K_{oc} = 68000 K_f = 1810 1/n = 1.08	Immobile.	Not reported	PMRA 1689035
		OC = 0.3%, pH 4.8, sandy loam.	K_d = 492 K_{oc} = 170000 K_f = 1010 1/n = 1.15	Immobile.	Not reported	PMRA 1689035
		OC = 2.5%, pH 4.8, silty clay loam.	K_d = 1320 K_{oc} = 52700 K_f = 2250 1/n = 1.12	Immobile.	Not reported	PMRA 1689035
		OC = 5.1%, pH 7.2, clay loam.	K_d = 1230 K_{oc} = 24200 K_f = 4380 1/n = 1.23	Immobile.	Not reported	PMRA 1689035
Soil column leaching	Tefluthrin	Speyer 2.1, 2.2 and 2.3 soils. Test 48 h duration. Elution 39.3 cm.	Not detected in leachate.	Immobile.	None reported	PMRA 1689035

		Aged residue column leaching. Acres sandy loam, Frenshem loamy sand soils. Aged 1 month. Test 6 weeks duration. Elution 66 cm in 6 weeks.	0.3% AR detected in leachate	Immobile.	Compound III 1.8% max, Compound IV 0.6% max Compound V 1% max. Recovery 43% and 69% AR, respectively, due to mineralization to CO_2 and possible volatilization of a.i. German Review (2006). PMRA Review (1993).	PMRA 1689035 PMRA Review (1993).
Field Studies						
Field dissipation	Tefluthrin	Champaign IL, silty clay loam 36.4% clay, 3.8% OM. 0–15 cm depth. PMRA Review (1993). Applied in May. Study duration 1 yr. TP <4%. Total rainfall 1182 mm. Active not detected below 10 cm. Application rate 2.24 kg a.i./ha. Peak recovery 7, 14 or 21 d after treatment. 10.3% (granular) & 11.8% (EC) carry over to year 2. Moderately persistent Dissipation linear first order model.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 100d DT_{90} = 300 d depth Emulsifiable concentrate DT_{50} = 106d DT_{90} = 318 d	Transformation products not reported	PMRA Review (1993).
		White Heath IL, silt loam pH 7.6, 22.4% clay, 2.3% OM. 0–15 cm depth. Applied in May. Study duration 1 yr. TP <4%. Total rainfall 1182 mm. Active not detected below 10 cm. Application rate 2.24 kg a.i./ha. Peak recovery 7, 14 or 21 d after treatment. 25.6% (granular) & 15.0% (EC) carry over to year 2. Dissipation linear first order model.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 79d DT_{90} = 237 Emulsifiable concentrate DT_{50} = 88d DT_{90} = 264 d	Transformation products not reported	PMRA Review (1993).
		White Heath IL, silt loam pH 6.0. Dissipation linear first order model. German Review (2006)	Emulsifiable concentrate DT_{50} = 100 d DT_{90} = 300 d	Transformation products not reported	PMRA 1689035
		Goldsboro NC, sandy loam Supplemental study pH 5.8, 7.8% clay, 2.4% OM. 0–15 cm depth. PMRA Review (1993). Applied in May. Study duration 1 yr. TP <4%. Total rainfall 1203 mm. Active not detected below 10 cm. Application rate 2.24 kg a.i./ha. Peak recovery 7, 14 or 21 d after treatment. 3.9% (granular) & 2.4% (EC) carry over to year 2. Linear first order model.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 29d DT_{90} = 87 d Emulsifiable concentrate DT_{50} = 45d DT_{90} = 135 d	Transformation products not reported	PMRA Review (1993).

		Vicksburg Miss, silt loam Supplemental study 14% clay, 1.1% OM. Application rate 779 g a.i./ha. Banded with press wheel partial incorporation. Study duration 215 d. Total rainfall 968 mm (>30 yr mean). 15.3% AR remained at end of study. Active not detected below 10 cm.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 66 d	Transformation products not reported	PMRA Review (1993).
		Vicksburg Miss, silt loam Supplemental study pH 6.4. 12% clay, 0.9% OM.. Study duration 215 d. <2% applied tefluthrin remained at 281 d. Rainfall 1333 mm. 95% AR detected in top 0–5cm. Volatilization <0.25% AR.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 24 d DT_{90} = 88 d DT_{50} = 26/26 granular (SFO/FOMC model).	Total transformation products <4% A.R.	PMRA Review (1993).
		Champaign IL, silty clay loam pH 7.6, 38.7% clay, 5.2% OM.. Study duration 215 d. 31% applied tefluthrin remained at 321 d. Rainfall 941 mm. TP <4%. 95% AR detected in top 0–5cm. Volatilization <0.25% AR.	Granular Appl. depth 1.3–2.5 cm DT_{50} = 70 d	Transformation products not reported	PMRA Review (1993).
		Champaign IL, sandy clay loam pH 7.6. Dissipation linear first order model.	Granular application DT_{50} =79 d DT_{90} = 237 d	Transformation products not reported	PMRA 1689035
		Champaign IL, sandy silt loam. Dissipation linear first order model.	Granular application DT_{50} = 165/84 d granular Estimated DT_{90} = 495 d assuming first order dissipation.	Transformation products not reported	PMRA 1689035
		London ON, sand muck and sandy clay loam. Study unacceptable. Various flaws. Force 1.0% a.i.	DT_{50} = NA	Transformation products not reported	PMRA Review (1993).
		Stoney Ck ON, sandy clay loam. 20.5% clay 2.4% OM. PMRA Review (1993). Force 1.5% a.i.. Banded application to surface of soil. Study unacceptable – not soil incorporated. Volatilization losses. Study duration 406 d. Applied in April. 14.6% AR carryover to next yr. Total rainfall 865 mm. No residues occurred below 20 cm.	Granular application not buried DT_{50} = 61 d. granular not buried	Transformation products not reported	PMRA Review (1993).
		Ormstown QC, clay loam Study unacceptable. Study duration 23 wk. 20% AR remained at wk 23. Force 1.0% a.i.. Application rate 750 g a.i./ha.	Granular application depth 3 cm DT_{50} = 70 d	Transformation products not reported	PMRA Review (1993).

Runoff Studies	Tefluthrin	Two small plots (0.065 ha each) simulated rainfall-watershed (flume) study Kentucky with T-banded application of Force 1.5G (75 g a.i./acre, 0.185 kg a.i./ha. Soil incorporated (2.5 cm depth) using spring tines. Tested yield of tefluthrin from gypsum base and clay base granules. Plot slopes 4.2–5.2%. Two simulated 1 in 5 yr rainstorm events at 4 and 11 d after application. Irrigation of 5.6 cm rainfall over 2 hours. Water yield 57% of applied rainfall (gypsum plot); 62% of applied (clay plot). Sediment yield gypsum granule plot 368 kg, clay granule plot 459 kg. Tefluthrin total (flow proportional) yield 121 mg a.i. (= 1.86 g a.i./ha, gypsum granule plot), 58 mg a.i. (= 0.89 g a.i./ha, clay granule plot). Mean tefluthrin conc on sediment 0.231 mg a.i./kg dw (gypsum plot), 0.086 mg a.i./kg dw (clay plot). Gypsum granule total yield 2 × higher than clay granule sed. conc. Conclusion: total transport ≤0.8% of applied.	Mean tefluthrin conc. on sediment (flow proportional) 0.231 mg a.i./kg dw gypsum 0.086 mg a.i./kg dw clay Total active yield (flow proportional) 0.385 kg a.i./ha gypsum 0.136 kg a.i./ha clay Total transported tefluthrin 0.1–0.7% of applied tefluthrin	Transformation products not reported	PMRA 1534109; 1534108; 1534107.
		Comparison of Force 3G and microencapsulated Force 30CS tefluthrin yield in simulated rainfall-watershed (flume) study in Kentucky. T-banded application rate 75 g a.i./acre (0.185 kg a.i./ha). Soil incorporated (2.5 cm depth) using spring tines. Two test plots (0.065 ha) each. Slopes 5.4% and 5.9%. Two simulated events, first 1 in 25–100 yr rainstorm event and 2nd 1 in 5 yr event on day at 2 and 9 after application. Irrigation of 11.2 cm rainfall over 4 hours. Natural rainfall 3.2 cm on day 3. Water yield 37% of applied (Force 3G plot) and 30% of applied (Force 30CS plot). Tefluthrin total (flow proportional 30 sec time interval yield 11.4 mg a.i. (= 0.175 g a.i./ha FORCE 3G) and 14.3 mg a.i. (= 0.220 g a.i./ha Force 30CS) (flow proportional sampling). Total tefluthrin transported 0.9% of applied (Force 3G plot) and 0.13% of applied (Force 30CS plot). Conclusion: total transport 0.15% of applied; transport of Force 3G 7 × higher than Force 30CS.	Total active yield (flow proportional) 0.175 kg a.i./ha Force 3G 0.220 kg a.i./ha Force 30CS Total transported tefluthrin (flow proportional) 0.9% of applied a.i.. Force 3G 0.13% of applied a.i.. Force 30CS	Transformation products not reported	PMRA 1534106

		Ten small watersheds Ohio, Miss., Iowa, each with pond, with 18 runoff events. One site had no significant runoff. Seven sites had runoff events with >50% of incident rainfall. 18 m buffer zone from pond. T-banded application of Force 1.5G at 0.185 kg a.i./ha. Soil incorporated (2.5 cm depth) using spring tines. Mean tefluthrin concentration in sediment 0.309ppm. Conclusion: for most events transported tefluthrin <0.5% of applied. In some events up to 3% of applied tefluthrin reached the pond after significantly intense event.	Tefluthrin runoff yield <0.5% applied for most events. Maximum tefluthrin yield 3% high intensity events	Transformation products not reported	PMRA 1534110.

* Transformation Product of Tefluthrin
Compound 1a – (1R,3R;1S,3S)-3-((Z)-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid.
Trans-tefluthrin – 2,3,5,6-tetrafluoro-4-methylbenzyl
Compound II – 2,3,5,6-tetrafluoro-4-methylbenzyl alcohol
Compound III – 2,3,5,6-tetrafluoro-4-methylbenzoic acid.
Compound IV – 2,3,5,6-tetrafluoroterephthalic acid.
Compound V – cis 1(RS),Z 4-{(3-[2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropyl)carbonyloxymethyl}-2,3,5,6-tetrafluorobenzoic acid

Table 3 Toxicity to Non-Target Species

Organism	Study type	Species	Test material	Endpoint*	Value (effect)	Effect of concern	Reference
Terrestrial Species							
Invertebrate	Acute oral	Honey bee (*Apis mellifera*)	Tefluthrin	48 h LD_{50}	1.73 µg a.i. /bee	Mortality	PMRA 1500084
	Acute contact	Honey bee (*Apis mellifera*)	Tefluthrin	48 h LD_{50}	0.16–0.28 µg a.i. /bee	Mortality	PMRA 1500084, 1596721
		Non-target Arthropods	Tefluthrin	NOEC seed treatment	10 g a.i./ha	Mortality	PMRA 1596721
	Acute contact	Earthworm (*Eisenia foetida*)	Tefluthrin	28 d LD_{50}	2.0 mg a.i./kg dry soil	Mortality	PMRA 1216954
		Earthworm (*Eisenia foetida*)	Tefluthrin	28 d NOEC	0.32 mg a.i./kg dry soil	Mortality	PMRA1216954
		Earthworm (*Eisenia foetida*)	Tefluthrin	Field Study NOEC	48 g a.i./ha	Mortality	PMRA 1596721
Birds	Acute oral	Bobwhite Quail (*Coturnix virginianus*).	Tefluthrin	LD_{50}	734 mg a.i./kg bw	Mortality	PMRA 1219059
		Mallard (*Anas platyrhynchos*)		LD_{50}	>3960 mg a.i./kg bw	Mortality	PMRA 1216930
		House Sparrow (*Passer domesticus*)		LD_{50}	267 mg a.i./kg bw	Mortality	PMRA 1216931
	Dietary	Bobwhite Quail (*Coturnix virginianus*).	Tefluthrin	LC_{50}	>10500 mg a.i./kg diet	Mortality	PMRA 1216933
		Mallard (*Anas platyrhynchos*)		LC_{50}	2317 mg a.i./kg diet	Mortality	PMRA 1216932
	Reproduction	Bobwhite Quail (*Coturnix virginianus*).	Tefluthrin	NOEC	25 mg a.i./kg diet	Mortality	PMRA 1216935; 1216941
		Mallard (*Anas platyrhynchos*)		NOEC	25 mg a.i./kg diet	Mortality	PMRA 1216934
Mammals	Acute oral	Rat	Tefluthrin	LD_{50}	21.8 mg a.i./kg bw (male) 34.6 mg a.i./kg bw (female)	Mortality	PMRA 1216629
	Dietary 90-day	Rat	Tefluthrin	NOAEL	7.5 mg a.i./kg bw/day (for both sexes)	Subchronic	PMRA 1216634

	Reproduction 2-generation	Rat	Tefluthrin	NOAEL	Parental 2.5 mg a.i./kg bw /day Reproductive 2.5 mg a.i./kg bw /day Offspring 0.75 mg a.i./kg bw /day	Reproduction	PMRA 1216663
Aquatic Species							
Freshwater Invertebrates	Acute	*Daphnia magna*	Tefluthrin technical	48-h EC_{50}	0.07 µg a.i./L	Immobility	PMRA 1216970
	Acute	*Daphnia magna*	Formulated product	48-h EC_{50}	2.1 µg a.i./L 7.9 µg formulation /L	Immobility	PMRA 1596721
	Chronic	*Daphnia magna*	Tefluthrin technical	21 d LC_{50} 21-d NOEC	0.00792 µg a.i. /L	Growth and reproduction	PMRA 1216945
Estuarine/marine Invertebrates	Acute	Mysid shrimp (*Mysidopsis bahia*)	Tefluthrin technical	96-h LC_{50}	0.053 µg a.i./L	Immobility	PMRA 1216971
Freshwater Fish	Acute	Rainbow trout (*Oncorhynchus mykiss*)	Tefluthrin technical	96-h LC_{50}	0.06 µg a.i./L	Mortality	PMRA1216968
	Acute	Bluegill sunfish (*Lepomis macrochirus*)	Tefluthrin technical	96-h LC_{50}	0.13 µg a.i./L	Mortality	PMRA1216969
	Acute	Mirror carp *(Cyprinus carpio)*	Tefluthrin technical	96-h LC_{50}	0.102 µg a.i./L	Mortality	PMRA 1596721
	Chronic (Early Life Stage)	Fathead minnow *(Pimephales promelas)*	Tefluthrin technical	28-d NOEC	0.0096µg a.i./L	Mortality	PMRA 1596721
	Chronic (Full Life Cycle)	Fathead minnow *(Pimephales promelas)*	Tefluthrin technical	300-d NOEC	0.00397µg a.i./L	Mortality	PMRA 1533960
Estuartine/marine Fish	Acute	Sheepshead minnows (*Cyprinodon variegatus*)	Tefluthrin technical	96-h LC_{50}	0.13 µg a.i./L	Mortality	PMRA 1216972
Freshwater Algae	Acute	Green alga (*Pseudokirchneriella subcapitata*)	Tefluthrin technical	96 h EC_{50}	>1.05 mg a.i./L	Growth rate	PMRA 1216943
			Tefluthrin technical	96 h EC_{50}	>1.05 mg a.i./L	Biomass	PMRA 1216943

Screening Level Risk Assessment Terrestrial Organisms

Table 4 Screening Level Acute Oral Risk to Birds from Consumption of Granules Containing Tefluthrin

Body weight (g)	FIR (g dw/d)	Application rate (g a.i./ha)	EDE (# gran/d) = FIR × # grand/g	Acute toxicity* granules/0.1 × LD_{50}	Acute RQ = EDE/Toxicity	LOC exceeded
20	5.1	112.5	108 579	379	287	Yes
20	5.1	150.0	108 579	379	287	Yes
100	19.9	112.5	423 671	1895	224	Yes
100	19.9	150.0	423 671	1895	224	Yes
1000	58.1	112.5	1 236 949	18950	65	Yes
1000	58.1	150.0	1 236 949	18950	65	Yes

gran/d = Number of granules consumed/day
gran/g = Number of granules/gram of product (FORCE®3.0G)
* Computed using toxicity for the house sparrow.

Table 5 Screening Level Reproductive Risk to Birds from Consumption of Granules Containing Tefluthrin

Body weight (g)	FIR g dw/d	Application Rate g a.i./ha	EDE (# gran/d) = FIR × #grand/g	Toxicity* granules/NOEL	Acute RQ = EDE/Toxicity	LOC Exceeded
20	5.1	112.5	108 579	20	5429	Yes
20	5.1	150.0	108 579	20	5429	Yes
100	19.9	112.5	423 671	100	4237	Yes
100	19.9	150.0	423 671	100	4237	Yes
1000	58.1	112.5	1 236 949	1001	1235	Yes
1000	58.1	150.0	1 236 949	1001	1235	Yes

gran/d = Number of granules consumed/day
gran/g = Number of granules/gram of product (FORCE®3.0G)
* Computed using chronic toxicity for the Bobwhite quail.

Table 6 Screening Level Acute Oral Risk to Mammals from Consumption of Granules Containing Tefluthrin

Body weight (g)	FIR g dw/d	Application Rate g a.i./ha	EDE (# gran/d) = FIR × #grand/g	Toxicity Granules/0.1 × LD_{50}	Acute RQ = EDE/Toxicity	LOC Exceeded
15	2.2	112.5	46 838	23.2	2019	Yes
15	2.2	150.0	46 838	23.2	2019	Yes
35	4.5	112.5	95 805	54	1774	Yes
35	4.5	150.0	95 805	54	1774	Yes
1000	68.7	112.5	1 462 623	1547	946	Yes
1000	68.7	150.0	1 462 623	1547	946	Yes

gran/d = Number of granules consumed/day
gran/g = Number of granules/gram of product (FORCE® 3.0G)

Table 7 Screening Level Reproductive Risk to Mammals from Consumption of Granules Containing Tefluthrin

Body weight (g)	FIR g dw/d	Application Rate g a.i./ha	EDE (# gran/d) = FIR × #grand/g	Toxicity Granules/NOEL	Acute RQ = EDE/Toxicity	LOC Exceeded
15	2.2	112.5	46 838	8.0	5855	Yes
15	2.2	150.0	46 838	8.0	5855	Yes
35	4.5	112.5	95 805	18.6	5151	Yes
35	4.5	150.0	95 805	18.6	5151	Yes
1000	68.7	112.5	1 462 623	532	2749	Yes
1000	68.7	150.0	1 462 623	532	2749	Yes

gran/d = Number of granules consumed/day
gran/g = Number of granules/gram of product (FORCE® 3.0G)

Table 8 Screening Level Risk to Earthworms from Tefluthrin

Row Width (cm)	Application Rate, g a.i./ha	EEC mg a.i./kg soil	Acute RQ = EEC/0.5 × EC_{50}	LOC (RQ ≥ 1)
75	112.5	0.050	0.05	Not exceeded
100	150.0	0.067	0.07	Not exceeded

Tox. Endpoint 0.5 × EC_{50} = 1.0 mg a.i./kg soil.

Refined Risk Assessment for Terrestrial Organisms

Table 9 Refined Acute Oral Risk to Birds from Consumption of Granules Containing Tefluthrin

BW (g) and guild	Application Rate g a.i./ha	EDE (# gran/d)	Toxicity* granules/ $LD_{50}^{5th\ percentile(50\%)}$	Acute RQ = EDE/Toxicity	LOC Exceeded
20 granivore/ominvore	112.5	25	472	0.05	No
20 granivore/ominvore	150.0	25	472	0.05	No
100 granivore/ominvore	112.5	25	2359	0.01	No
100 granivore/ominvore	150.0	25	2359	0.01	No
1000 nongranivore	112.5	70 000†	112 065	0.6	No
1000 granivore	150.0	750‡	23 585	0.001	No
1000 nongraivore	112.5	70 000†	112 065	0.6	No
1000 granivore	150.0	750‡	23 585	0.001	No

gran/d = Number of granules consumed/day

* Computed using small sample $LD_{50}^{5th\ percentile(50\%)}$ from SSD = 157.9 mg a.i./kg bw. For 20 g, 100 g and 1000 g granivores and omnivores acute toxicity = $LD_{50}^{5th\ percentile(50\%)}$ × BW (kg) / 0.006695 mg a.i./granule. For 1000 g granivores acute toxicity = $LD_{50}^{5th\ percentile(50\%)}$ × BW (kg) / 0.001409 mg a.i./granule.

† Based on Luttik and de Snoo's (2004) data for Mallard

‡ Based on Luttik and de Snoo's (2004) data for Pheasant

Table 10 Refined Reproductive Risk to Birds from Consumption of Granules Containing Tefluthrin

BW (g) and guild	Application Rate g a.i./ha	Maximum EDE (# gran/d)	Toxicity* granules/ $NOEL^{5th\ percentile(50\%)}$	Acute RQ = EDE/Toxicity	LOC Exceeded
20 granivore/ominvore	112.5	25 (4.3)§	1	25 (4.3)§	Yes
20 granivore/ominvore	150	25 (4.3)§	1	25 (4.3)§	Yes
100 granivore/ominvore	112.5	25 (4.3)§	5	5 (0.9)§	No
100 granivore/ominvore	150.0	25 (4.3)§	5	5 (0.9)§	No
1000 nongranivore	112.5	70,000†	234	299	Yes
1000 granivore	150.0	204‡ (35)§	49	4.2 (0.7)§	No
1000 nongraivore	112.5	70,000†	234	299	Yes
1000 granivore	150.0	204‡ (35)§	49	4.2 (0.7)§	No

gran/d = Number of granules consumed/day

* Computed using small sample $NOEL^{5th\ percentile(50\%)}$ from SSD = 0.33 mg a.i./kg bw. For 20 g, 100 g and 1000 g granivores and omnivores chronic toxicity = $NOEL^{5th\ percentile(50\%)}$ × BW (kg) / 0.006695 mg a.i./granule. For 1000g granivores chronic toxicity = $NOEL^{5th\ percentile(50\%)}$ × BW (kg) / 0.001409 mg a.i./granule.

† Based on Luttik and de Snoo's (2004) data for Mallard

‡ Based on Luttik and de Snoo's (2004) data for Pheasant

§ Value in brackets are risk quotients further reduced based on 6:1 preference factor silica grit to baked clay (*i.e.* EDE = (1/6) × 25 = 4.3 granules)

Table 11 Refined Acute Oral Risk to Mammals Based on Percent Mineral Matter in the Diet

BW (g)	Application Rate g a.i./ha	EDE (# gran/d) × % mineral matter in diet*	Toxicity* granules/ $LD_{50}^{5th\ percentile(50\%)}$	Acute RQ = EDE/Toxicity	LOC Exceeded
15	112.5	1124	59	19	Yes
15	150.0	1124	59	19	Yes
35	112.5	2299	139	16	Yes
35	150.0	2299	139	16	Yes
1000	112.5	92145	3960	23	Yes
1000	150.0	92145	3960	23	Yes

gran/d = Number of granules consumed/day

* 2.4% mineral matter for 15g and 35 g mammals and 6.3% for 1000 g mammals.

Table 12 Refined Reproductive Risk to Mammals Based on Percent Mineral Matter in the Diet

BW (g)	Application Rate g a.i./ha	EDE (# gran/d) × % mineral matter in diet*	Toxicity* granules/ $NOEL^{5th\ percentile(50\%)}$	Acute RQ = EDE/Toxicity	LOC Exceeded
15	112.5	1124	2	562	Yes
15	150.0	1124	2	562	Yes
35	112.5	2299	4.7	489	Yes
35	150.0	2299	4.7	469	Yes
1000	112.5	92145	135	683	Yes
1000	150.0	92145	135	683	Yes

gran/d = Number of granules consumed/day

* 2.4% mineral matter for 15g and 35 g mammals and 6.3% for 1000 g mammals.

Screening Level Risk Assessment for Aquatic Organisms

Table 13 Screening Level Acute Risk to Freshwater Fish from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ $EEC/(0.1 \times LC_{50})$	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	2350	Yes
150	0.80	0.0188	3133	Yes

Table 14 Screening Level Risk to the Life Cycle of Freshwater Fish from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/(NOEC)	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	3552	Yes
150	0.80	0.0188	4735	Yes

Table 15 Screening Level Acute Risk to Freshwater Invertebrates from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ $EEC/(0.5 \times LC_{50})$	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	403	Yes
150	0.80	0.0188	537	Yes

Table 16 Screening Level Risk to the Life Cycle of Freshwater Invertebrates from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/NOEC	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	1780	Yes
150	0.80	0.0188	2374	Yes

Table 17 Screening Level Acute Risk to Amphibians from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
112.5	0.15	0.075	12500	Yes
150	0.15	0.100	16667	Yes

Table 18 Screening Level Risk to the Life Cycle of Amphibians from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
112.5	0.15	0.075	20270	Yes
150	0.15	0.100	27027	Yes

Table 19 Screening Level Acute Risk to Estuarine/Marine Fish from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	1084	Yes
150	0.80	0.0188	1446	Yes

Table 20 Screening Level Acute Risk to Estuarine/Marine Invertebrates from Tefluthrin

Application Rate g a.i./ha	Water Depth m	EEC Direct Application mg a.i./L	Acute RQ EEC/(0.5 × LC_{50})	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	532	Yes
150	0.80	0.0188	709	Yes

Table 21 Screening Level Acute Risk to Algae from Tefluthrin

Application Rate g a.i./ha	Water Depth M	EEC Direct Application mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
112.5	0.80	0.0141	0.013	No
150	0.80	0.0188	0.018	No

Refined Risk Assessment on Non-Target Aquatic Species

Table 22 Acute Risk to Freshwater Fish from Tefluthrin in Runoff

Scenario	Appl.Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.00013 peak value	22	Yes
ON Corn	22.5	0.80	0.000039 peak value	6.5	Yes
ON Corn	22.5	0.80	0.000008 96h value	1.3	Yes
QB Corn	22.5	0.80	0.000008 96h value	1.3	Yes
MN Corn	22.5	0.80	0.0000089 96h value	1.5	Yes
P.E.I. Corn	22.5	0.80	0.00003 96h value	5.0	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 23 Risk to the Life Cycle of Freshwater Fish from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(NOEC)	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.00001 Yearly value	2.5	Yes
ON Corn	22.5	0.80	0.000002 Yearly value	0.5	No
QB Corn	22.5	0.80	0.000003 Yearly value	0.8	No
MN Corn	22.5	0.80	0.0000028 Yearly Value	0.7	No
P.E.I. Corn	22.5	0.80	0.000007 Yearly Value	1.8	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 24 Acute Risk to Freshwater Invertebrates from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.5 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.00013 peak value	3.7	Yes
ON Corn	22.5	0.80	0.000039 peak value	1.1	Yes
ON Corn	22.5	0.80	0.000008 96 h value	0.2	No
QB Corn	22.5	0.80	0.000008 96 h Value	0.2	No
MN Corn	22.5	0.80	0.0000089 96 h Value	0.3	No
P.E.I. Corn	22.5	0.80	0.00003 96 h Value	0.9	No

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 25 Risk to the Life Cycle of Freshwater Invertebrates from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/NOEC	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.000017 21 d Value	2.2	Yes
ON Corn	22.5	0.80	0.000004 21 d Value	0.5	No
QB Corn	22.5	0.80	0.000004 21 d Value	0.5	No
MN Corn	22.5	0.80	0.000004 21 d Value	0.5	No
P.E.I. Corn	22.5	0.80	0.000013 21 d Value	1.6	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 26 Acute Risk to Amphibians from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.15	0.00068 Peak Value	113	Yes
QB Corn	22.5	0.15	0.0002 Peak Value	33	Yes
ON Corn	22.5	0.15	0.000033 96 h Value	5.5	Yes
QB Corn	22.5	0.15	0.000035 96 h Value	5.8	Yes
MN Corn	22.5	0.15	0.000037 96 h Value	6.6	Yes
P.E.I. Corn	22.5	0.15	0.00013 96 h Value	22	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 27 Risk to the Life Cycle of Amphibians from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.15	0.000026 60 d Value	6.5	Yes
QB Corn	22.5	0.15	0.000006 60 d Value	1.5	Yes
ON Corn	22.5	0.15	0.000002 Yearly Value	0.5	No
QB Corn	22.5	0.15	0.000003 Yearly Value	0.8	No
MN Corn	22.5	0.15	0.000003 Yearly Value	0.8	No
P.E.I. Corn	22.5	0.15	0.000089 Yearly Value	2.2	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 28 Acute Risk to Estuarine/Marine Fish from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.1 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.00013 peak value	10	Yes
ON Corn	22.5	0.80	0.000039 peak value	3.0	Yes
ON Corn	22.5	0.80	0.000008 96h value	0.6	No
QB Corn	22.5	0.80	0.000008 96h value	0.6	No
MN Corn	22.5	0.80	0.0000089 96h value	0.7	No
P.E.I. Corn	22.5	0.80	0.00003 96h value	2.3	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

Table 29 Acute Risk to Estuarine/Marine Invertebrates from Tefluthrin in Runoff

Scenario	Application Rate g a.i./ha	Water Depth m	EEC Runoff mg a.i./L	Acute RQ EEC/(0.5 × LC_{50})	LOC (RQ ≥ 1) Exceeded
P.E.I. Potato level 1*	22.5	0.80	0.00013 peak value	4.9	Yes
ON Corn	22.5	0.80	0.000039 peak value	1.5	Yes
ON Corn	22.5	0.80	0.000008 96 h value	0.3	No
QB Corn	22.5	0.80	0.000008 96 h Value	0.3	No
MN Corn	22.5	0.80	0.0000089 96 h Value	0.3	No
P.E.I. Corn	22.5	0.80	0.00003 96 h Value	1.1	Yes

Application rate = 15% × 150 g a.i./ha applied = 22.5 g a.i./ha amount of tefluthrin exposed at the surface available for runoff

* Potato is not a registered use in Canada; however, it is included as the worst use scenario for modeling purpose.

Appendix VIII Label Amendments for Commercial Class Products Containing Tefluthrin

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the label statements given below.

A submission to request label revisions will be required within 90 days after the re-evaluation decision is finalized.

The Canadian commercial end-use product label must be amended to include the following statements to further protect workers and the environment.

I) The following statements must be included in the **PRECAUTIONS** section:

> "Keep the following personal protective equipment immediately available for use in case of emergency (*i.e.* a broken package, spill, or equipment breakdown): chemical-resistant coveralls, chemical-resistant gloves, chemical-resistant head gear and a respirator."

II) The following statements must be included in the **DIRECTIONS FOR USE** section.

- Rotational crops may be planted no sooner than 30 days after application.
- Do not harvest sweet or field corn for forage until 49 days after treatment and for cobs or grain until 56 days after treatment.

Engineering Controls and Personal Protective Equipment

A. Mixing and loading granules:
Open mixing and loading with maximum Personal Protection Equipment (PPE): Chemical resistant coveralls over a single layer (long-sleeved shirt, long pants, socks plus shoes) with chemical resistant gloves, plus a suitable respirator.

B. Applying granules by tractor drawn broadcast spreader:
Use a closed cab with maximum Personal Protection Equipment (PPE): Chemical resistant coveralls over a single layer (long-sleeved shirt, long pants, socks plus shoes). Add chemical resistant gloves for all tasks outside of the closed cab.

Restricted-entry Intervals

Observe a restricted-entry interval of 12 hours after application for all postapplication activities.

III) The following statements must be included in the **ENVIRONMENTAL HAZARDS** section:

- **TOXIC** to aquatic organisms.
- **TOXIC** birds and small wild mammals. Any spilled or exposed granules must be incorporated into the soil or otherwise cleaned-up from the soil surface.

RUN-OFF

To reduce runoff from treated areas into aquatic habitats, avoid application to areas with a moderate to steep slope, compacted soil or clay.

Avoid application when heavy rain is forecast.

Contamination of aquatic areas as a result of runoff may be reduced by including a vegetative strip between the treated area and the edge of the water body.

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